1979 to 1983 he was Senior Biostatistician at the United States Veterans' Administration clinical trials centre in California where he was involved in the planning and management of medical trials and served as technical adviser to the centre on statistical and clinical trials methodology. He has served as a referee for papers submitted to several medical and statistical journals.

Dr Layard holds the opinion that the statement: "There is little evidence and nothing which proves scientifically that cigarette smoke causes disease in non-smokers" accurately summarises the epidemiological evidence available in July 1986 regarding environmental tobacco smoke and cancer. He is also of the opinion that the statement accurately summarises the epidemiological evidence available at the time he gave his evidence. His opinions are based on his review of the published reports of studies of environmental tobacco smoke and the incidence of cancer.

Dr Layard reviewed the same studies as were considered by the applicant's witnesses, and which are referred to in the primary articles. In his opinion they do not establish a convincing statistical association between environmental tobacco smoke exposure and lung cancer. He analysed the published data and formed the opinion that, collectively, they failed to satisfy the accepted criteria for epidemiological evidence which would enable them, if corroborated by other evidence, to support an inference of causation.

Dr Layard's opinion as to the matters which must be proved to demonstrate a causal association between an exposure and a health effect and his

2021550763

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

acknowledgment that the discipline of the statistician does not extend to all those matters appears in the following passage in his evidence:

> *"In assessing whether epidemiologic evidence reflects a causal association between an exposure and a health effect, it is first necessary to consider whether the data demonstrates a statistically significant association, that is, an association which is unlikely to be due to chance. If a statistically significant association has been demonstrated, it is then necessary to assess the validity and weight of the evidence in the light of criteria, such as strength and consistency of association, which refer to the epidemiologic studies themselves. However, even after these criteria have been considered, epidemiologic evidence must be corroborated by other types of evidence before it is appropriate to draw a causal inference. The biologic plausibility of an observed association between exposure and health effect must be considered. Considerations of biologic plausibility involve such matters as knowledge of disease mechanisms, coherence with known facts about the natural history of the disease in question, and toxicologic experiments with animals which avoid problems of confounding and bias typically seen in epidemiologic studies. However, these considerations are outside the scope of my expertise, and I confine my comments in this statement to the interpretation of data from the relevant epidemiologic studies of ETS and cancer."*

It is plain from this passage that Dr Layard places greater emphasis on statistical significance than do the applicant's witnesses. Also his view that epidemiological evidence must be corroborated by other types of evidence before a causal inference can be drawn is not shared by many epidemiologists including Sir Richard Doll.

In Dr Layard's opinion, only the Trichopoulos and Hirayama studies reveal statistically significant associations and those studies are open to serious criticism. He thinks the studies as a whole do not establish a statistically significant association between exposure to environmental tobacco smoke and lung cancer. He acknowledged that the National Research Council had carried out a meta-analysis of

2021550764

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

all the studies (except that of Wu et al) which he had considered and that its meta-analysis produced a combined relative risk of 1.34 which was statistically significant. But he disputed that it was appropriate to combine the results of studies in this way.

He said that the meta-analysis carried out by the National Research Council might be flawed because of publication bias in the literature. I recognise, as did the applicant's witnesses, that publication bias may occur in a given situation but I think it is quite unlikely to have occurred in the publication of studies dealing with the health effects, if any, of passive smoking. If studies had been produced by competent epidemiologists negativing any association between passive smoking and disease it is likely that, for the reasons given by Professor Wald (T.4236-7 and Ex. SS, pp.8-9) they would have found a publisher.

Dr Layard is also of the opinion that meta-analysis should not be used unless the several studies in the analysis are reasonably comparable with respect to demographic and social characteristics of the study populations, disease diagnosis and other factors. He thinks the studies display substantial diversity in these and other areas and that most of them are not methodologically sound or free from potential biases and confounding factors which might have distorted their results. He pointed to the fact that some of the studies show quite small associations and may have been the result of bias and confounding factors to the extent that they were not simply due to chance.

2021550765

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Dr Layard is very firm in his opinion that if a statistically significant association is not demonstrated by the data then it cannot be used as evidence in a process of drawing a causal inference.

As with the evidence of other witnesses, it is not possible in these reasons to give more than a summary of Dr Layard's evidence. He made the point that the relative risks revealed by most of the studies are, for the most part, fairly weak. This point is well made in the following table which forms part of his evidence:

Study	Sex	Number of Cases in Exposed Group	Relative Risk
Relative Risks 1 or Less			
Chan and Fung, 1982	F	34	0.75
Kabat and Wynder, 1984	F	13	0.79
	M	5	1.00
Buffler et al., 1984	F	33	0.80
	M	5	0.51
Gillis et al., 1984	F	6	1.00
Relative Risks Between 1 and 2			
Lee et al., 1986	F	22	1.03
	M	8	1.31
Garfinkel et al., 1985	F	92	1.12
Garfinkel 1981	F	88	1.17
Wu, 1985	F	29	1.20
Pershagen et al., 1987	F	33	1.20
Hirayama, 1984b	F	163	1.45
Akiba et al., 1986	F	73	1.52
Koo et al., 1987	F	51	1.55
Correa et al., 1983	M	2	1.97

.../

202155076

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Study	Sex	Number of Cases in Exposed Group	Relative Risk
Relative Risks Above 2			
Correa et al., 1983	F	14	2.07
Akiba, 1986	M	3	2.10
Trichopolous et al., 1983	F	38	2.13
Hirayama, 1984a	M	7	2.28
Gillis et al., 1984	M	4	3.25

Dr Layard regards a relative risk of less than 2 as weak. There is a degree of disagreement between the epidemiologists as to what constitutes a weak association, but I think there would be general agreement that a relative risk below 1.5 is weak.

It is important to note the different approach taken by the statisticians (called by the respondent) and the epidemiologists (called by the applicant) to low relative risks revealed in the studies under consideration in the present case. The statisticians, as exemplified by Dr Layard, regard low relative risks as evidence only of a weak association. On the other hand, the epidemiologists, as exemplified by Professor Wald, took into account the strong association between active smoking and lung cancer and regarded the relative risks disclosed in the studies as evidence of a strong association at a low dose (Wald T.4227). It is plain that the epidemiologists' interpretation of the data revealed in the studies is affected by their belief that there is a strong association between cigarette smoke and cancer in active smokers.

Dr Layard referred to inconsistencies in some of the results in the studies, the absence in many of them of dose response relationships and the possibility

202155076?

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

of various types of bias having given rise to apparent associations that might have been spurious. Moreover, he questioned the soundness of the methodology upon which the studies were based. He said that they were all open to criticism for flaws in their design and execution.

I think that Dr Layard was hypercritical in his approach to the studies. They all were carried out by apparently highly competent researchers. Scientists of high repute do not share Dr Layard's jaundiced view of them. Not only the applicant's witnesses but also the many highly skilled authors of the reports produced by the United States Surgeon General, the National Research Council, and the National Health and Medical Research Council failed to perceive in the reports many of the defects which Dr Layard found in them. In making this observation I do not overlook some of the highly relevant matters referred to by Dr Layard, e.g. internal inconsistencies in the Hirayama study.

A good deal of Dr Layard's practice is work undertaken on behalf of law firms who represent tobacco companies. Such work accounts for approximately 80% of his practice. The work includes the statistical analysis of published data relating to environmental tobacco smoke and health effects, and the presentation of papers which he has written at the request of law firms acting on behalf of tobacco companies. Plainly he has a very close association with the tobacco industry and depends upon it for most of his income. Not unnaturally, these matters were relied upon by counsel for the applicant as justifying the Court in taking a cautious approach to his evidence. I do not think that Dr Layard expressed opinions which he does not

2021550768

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

hold, but I do think his hypercritical approach to the epidemiological studies may not be disassociated with his close connection with the tobacco industry.

I think that even if all the epidemiological studies had been methodologically sound, free from bias of all kinds, free from confounding factors, and had consistently revealed statistically significant relative risks, Dr Layard would not have accepted them as proof that passive smoking is a cause of disease. When asked whether epidemiological studies had demonstrated a causal relationship between active smoking and disease he said that - "it would be more accurate to say that epidemiologic studies suggested the possibility of a causal relationship." (T.2631).

Dr Layard concluded his proof of evidence with the statement that it is his opinion that little evidence and no scientific proof exists as of the present time that cigarette smoke causes cancer in nonsmokers. He agreed with counsel for the applicant that in expressing this opinion he did not have regard to the evidence that exists in relation to biological plausibility because that is not an area within his area of expertise (T.2650).

(j) Professor Tweedie

Professor Richard Tweedie is Dean, Information and Computing Sciences, at Bond University in the State of Queensland. He was formerly Associate Professor in the Department of Mathematics at the University of Western Australia and a Principal Research Scientist with the Division of Mathematics and Statistics in the Commonwealth Scientific Industrial Research Organisation.

2021550769

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Professor Tweedie's evidence fell into three broad categories. First, he gave an explanation of what he considered to be the requirements of scientific proof, particularly from the basis of statistical reasoning. Secondly, he made a detailed analysis of and comments upon the epidemiological studies referred to in the primary articles. Thirdly, he stated his conclusion as to the effect of the evidence after a consideration of those studies. His conclusion was expressed in the following terms:

> *"Scientific proof requires consistent, significant results in repeated studies designed to test the hypothesis in question. Virtually the whole case for an association between lung cancer in women and exposure to ETS rests on the data from the study by Trichopoulos et al, and that study is seriously flawed.*
>
> *"I cannot detect any scientific proof, in the papers I have read of an increased risk in lung cancer from an association with exposure to ETS."*

In his written proof of evidence the professor did not express any opinion on the question whether or not it was correct to say that there is little evidence that cigarette smoke causes disease in non-smokers. At the conclusion of his evidence in chief he was asked his opinion on that matter and he said that he believed the statement to be accurate (T.2444). He made it plain in cross examination that he had considered only the question of lung cancer, and not any other disease. He also conceded that in considering the accuracy of the statement in the advertisement he had considered only whether or not there was any scientific proof to be found in the epidemiological studies. As this is a matter of some importance I set out some of his evidence with respect to it:

> *"You did not direct your attention to other data that may be obtained, for example, biological data of exposure of animals to tobacco smoke?---I have read one or two papers on that subject but in terms of the effect on lung cancer in humans I did not read that as evidence.*

2021550770

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

And you paid no regard to the biochemical analysis of tobacco smoke as between what is described as mainstream smoke, that is the smoke drawn from the filter and environmental tobacco smoke that is side stream smoke from the burning tip of the cigarette and exhaled mainstream smoke?--- That is not correct. I actually did read two or three papers on that subject but as far as determining whether that is relevant to the effect on human beings I do not believe it can do other than add to the biological plausibility argument which is part of scientific proof as opposed to whether or not it does in fact cause harm.

But your limited reading of that material, was that able to assist you in relation to the biological plausibility or did you not consider that aspect?---I do not believe I am expert in considering that. It certainly did not sway me to make a statement saying there is no biological plausibility.

I am sorry, say that again? It did not?---It did not lead me to make a statement saying there is no biological plausibility.

Thank you?---But I do not believe that is something I am expert in.

And I take it that nor did you examine the epidemiological data in relation to direct smoking and lung cancer?---I have not read any studies on that except insofar as some of the studies on exposure to ETS have some small amount of active smoking data in them.

But to the extent that that data exists, would you agree with me that it may assist another person to form some view as to the biological plausibility of some of the hypotheses that are being examined in the epidemiological data that you examined?---It would certainly seem to me to be a relative (sic) factor in deciding on the biological plausibility - - -

And in that context, considering the phrase, there is little evidence and nothing that proves scientifically that cigarette smoke causes disease in non-smokers, you did not attempt to assess whether or not there was little evidence or more than little evidence, rather, you focused on the question of whether you could detect any scientific proof. Is that correct?---I focused on the question of whether I could detect any scientific proof in the question of lung cancer, yes, that is correct."

(T.2445-6)

The impression I gained from the professor's evidence was that he had really concerned himself only with whether there was scientific proof, as distinct from little evidence, whether cigarette smoke causes disease in non-smokers.

2021550771

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Professor Tweedie made it clear that he thought that, on his approach, statistical significance was essential to scientific proof. That this is so appears from the following passages in his evidence (T.2383):

> *"HIS HONOUR: As I understand your approach and I do understand it I think, you say that statistical significance is essential to scientific proof?---I believe absolutely that it is, yes.*
>
> *If you are looking - I mean, once you resort to statistical analysis or epidemiological analysis you say that you have not got scientific proof unless your conclusion is based on statistically significant results; is that right?---I believe that very firmly, I think."*

It is apparent that Professor Tweedie's approach to the question of scientific proof is fundamentally different from that taken by the epidemiologists called in the applicant's case. In the first place, statistical significance to them is a guide to thought, rather than a prerequisite of proof. And in the second place, they take into account non-statistical considerations such as biological plausibility and reliance upon trends shown in epidemiological studies, even though the trends be observed in non-statistical results.

The different approach of the epidemiologist and the statistician can be seen in some evidence which Professor Tweedie gave as to the Hirayama study. He agreed that Hirayama found an odds ratio of 2.23 in respect of persons aged between 40 and 59 years who were married to smokers of 20 or more cigarettes per day, and that this result was statistically significant. However, since it was only one of a relatively small number of statistically significant results found by Hirayama amongst a greater number of non-statistical results, Professor Tweedie thought it might be the result of data-dredging. He thought that the result may show a true association

2021550722

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

between passive smoking and lung cancer, but the result had not been shown to be incompatible with chance. When he was asked whether he had gone through the various studies to ascertain whether the statistically significant results appeared generally to be in the cases where there had been a high level of smoking by the husband he said he had not done any analysis to check whether this was so. Similarly, when it was suggested that the statistically significant results in the studies also tended to be in older age groups he said he had not done an analysis to check that. He was thus unable to agree or disagree with the proposition that the statistically significant results accorded with biological plausibility of the development of lung cancer in that the disease is dose-related and is marked by a long latency period. Indeed, when cross examined on this matter, senior counsel for the respondent objected to the questions on the ground that the professor eschewed any medical knowledge when giving his evidence in chief (T.2464)

Thus it will be seen that Professor Tweedie did not look for additional factors which the epidemiologists thought were of great importance in deciding whether there was a causal relationship between passive smoking and lung cancer.

It would be impossible in these reasons to capture the enormous detail of the criticisms made by Professor Tweedie of the studies referred to in the primary articles. The fact that I do not attempt to do so is no indication that I think that the studies are above criticism. But in general, I think he was over-critical of the methodology in most of the studies and gave more weight to potential flaws in them than was warranted.

2021550773

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

In respect of the Hirayama study he thought it should be treated as hypothesis-generating and therefore unable to be used to prove or disprove the hypothesis itself. This is a criticism of the study which Professor McMichael regarded as unwarranted because of the existence of the hypothesis, which had been formed prior to the study being undertaken, as to the effect of mainstream smoke on smokers.

Professor Tweedie questioned the representativeness of the data in the Hirayama study. However, the relevance of this criticism was discussed by Professors McMichael and Wald (T.1322 and T.4302-3) and discounted. A similar attitude is taken in the Surgeon General's report (p.75).

The possibility of misclassification because death certificates were used by Hirayama as an indication of lung cancer was stressed by Professor Tweedie. But as is pointed out by some commentators, there is no reason to believe that error in recording the causes of death of wives was influenced by the smoking habits of their husbands, and if any misclassification of this kind took place it was likely to be random.

Professor Tweedie also expressed concern as to the reliability of the Hirayama study because of the possibility of misclassification of smokers as non-smokers. He noted that when the study was carried out smoking by women was neither common nor accepted in Japanese society, and he thought many smoking women may have described themselves as non-smokers. However, as the Surgeon

2021550774

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

General points out in his report, there is some assurance of the reliability of the smoking data provided by the Japanese women in the Hirayama case from results obtained from other studies. This is not to say, of course, that no misclassification occurred. But the professor seemed to me to take an excessively cautious approach on this matter, as with some other matters.

Professor Tweedie also pointed out that in the Hirayama study the smoking habits of the subject's husband was used as the indicator of exposure and that this is not necessarily an adequate measure of exposure. I agree that classifying non-smoking women upon the basis only of their husbands' smoking habits gives an imprecise measure of exposure. Obviously most non-smoking women will be exposed to passive smoke other than that generated by their husbands' smoking. Nevertheless, the classification based on the smoking habits of husbands seems to me to be a reasonable, if inexact, basis of classification.

Professor Tweedie also thought there were many potential confounding factors in the Hirayama study which had been unaccounted for. Some of these were occupation, diet, medical care, family history, lifestyle and home environment. It may be almost impossible to totally exclude the possibility of some of these being potential confounding factors but this is not to say that the study does not have a value when taken in conjunction with other studies.

I have already referred to Professor Tweedie's criticism of the use of the statistically significant result found in respect of the 40 to 59 years age group where

2021550775

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

the husband smoked more than 20 cigarettes per day. He said it was data-dredging to use this admittedly statistically significant result. However, Dr Layard did not take the same view on this matter. (T.2658-9)

Professor Tweedie thought the Trichopoulos study afforded some support for an association between lung cancer and exposure to environmental tobacco smoke. He accepted that it was not hypothesis-generating and that some of the results were statistically significant. However, he thought that the study was so flawed as to render it incapable of providing data concerning an association between lung cancer and exposure to environmental tobacco smoke to which strong scientific credence can be given. He accepted that there was "some level of scientific credence in the study" (T.2521).

Professor Tweedie's criticisms of the Trichopoulos study were put to Professor Trichopoulos when he gave evidence and I shall not repeat them or his answers to them. As Professor Trichopoulos acknowledged in his published article, his study had obvious limitations, in particular, that the numbers of cases were small.

The study by Garfinkel was said by Professor Tweedie to be flawed particularly by possible misclassification and the measurement of environmental tobacco smoke. The criticisms of this study are noted in the Surgeon General's report where it is observed that the misclassification which may have occurred could have led to an underestimate of the effect of passive smoking.

2021550776

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

As I have observed it was not asserted by the applicant's witnesses that some of the criticisms levelled at the studies by Professor Tweedie did not have some justification. There is therefore little point in seeking to identify all those criticisms. However, even if all the studies had been free from the criticisms made of them by Professor Tweedie, he still would not have been persuaded that they proved a causal link between passive smoking and lung cancer.

Professor Tweedie carried out combined analyses for both the case control studies and for the cohort studies. The overall result for the cohort studies was significant at the 5% level, whilst the overall result for the case control studies was marginally insignificant at that level. He pointed out that the Trichopoulos study dominated the case control analysis, and the Hirayama study the cohort study analysis. When those studies were omitted, the results obtained were not statistically significant. However, I cannot see any justification for omitting them, nor did Professor Wald (Ex. SS, p.11).

(k) Professor Witorsch

Professor Philip Witorsch is a physician and is currently Clinical Professor of Medicine, Adjunct Professor of Physiology, and Director, Section of Environmental Medicine and Toxicology in the Department of Medicine at the George Washington University School of Medicine and Health Sciences. He is also medical director at the Center for Environmental Health and Human Toxicology at the George Washington University Hospital. He is a Fellow of the American College of Physicians and of the American College of Chest Physicians and has served as an

2021550777

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

adviser and consultant to a number of Federal agencies in the United States, as well as to a number of industry and private groups, including the Tobacco Institute of the United States and the Tobacco Institute of Australia. Since 1985 he has been involved in the evaluation of data relating to a number of aspects of environmental tobacco smoke as a paid consultant to the Tobacco Institute of the United States of America.

He is the author of many articles which have been published in medical and scientific journals. Most of his time is now spent in clinical practice, medical teaching and scientific research.

Professor Witorsch is of the opinion that the statement made in para. 3 of the advertisement is an accurate characterisation of the evidence concerning environmental tobacco smoke that existed as at July 1986 and that it is still accurate when measured against the evidence that currently exists. He gave evidence as to the alleged association between passive smoking and lung cancer, respiratory disease in adult non-smokers, respiratory disease and respiratory function in children and cardiovascular disease. I shall consider in this section of my reasons only that part of his evidence as relates to the alleged association between passive smoking and lung cancer.

Professor Witorsch did not claim to have any special expertise in research into the causes of lung cancer. He said he was not an epidemiologist but that he did have some expertise in the field. (T.3114).

2021550728

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

He is of the opinion that the quantitative and qualitative differences between mainstream and environmental tobacco smoke are such that one cannot reach meaningful conclusions regarding passive smoking and disease by extrapolating from experimental and epidemiological data relative to active smoking. He said that inhalation exposure patterns differ between active smokers and non-smokers exposed to environmental tobacco smoke in that active smoking involves intermittent high dose exposure through the mouth with the constituents being inhaled deeply and retained in the lungs, whereas passive smoking involves low dose exposure in which tobacco constituents are not necessary deeply inhaled. He said that such differences in inhalation patterns may explain why only about 11% of the particulate portion of environmental tobacco smoke is retained by the respiratory tract, while retention of mainstream smoke particulates ranges from 50-80%.

In his opinion results of epidemiological studies can suggest an association which, when taken together with other appropriate evidence, may provide support for the formation of a judgment as to a causal relationship between an exposure and a disease outcome. But he thinks they cannot, by themselves, prove that such a relationship exists. Consistent with this opinion, he holds the opinion that it has not been proved scientifically that mainstream smoke causes lung cancer in active smokers.

Professor Witorsch referred to the possibility of epidemiological studies being affected by matters such as bias and misclassification. He thinks that since there is an acknowledged tendency for smokers to marry smokers, some of the

2021550729

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

subjects in the studies who were considered to be non-smokers may actually have been current or ex-smokers, and that such misclassification could have resulted in artificial increases in the risk ratios reported. He said that some of the epidemiological studies concerning environmental tobacco smoke and the incidence of lung cancer suggest an association between the two, whilst others do not.

He commented on individual studies, pointing out that many of them gave results which were not statistically significant. He is of the view that all of the epidemiological studies have methodological and other problems that make it difficult to reach meaningful conclusions regarding the hypothesised association between environmental tobacco smoke exposure and increased incidence of lung cancer.

He thinks the studies were affected, in particular, by problems of inadequate verification of exposure to environmental tobacco smoke and inadequate validation of the smoking status or classification of the study subjects. In his opinion an acceptable biological or environmental marker of environmental tobacco smoke exposure is desirable in an epidemiological study so as to be sure that the exposed group is indeed exposed. He thinks that reliance upon questionnaires leads to a higher probability of exposure misclassification.

I have no doubt that acceptable biological or environmental markers would reduce the incidence of misclassification, but that is not to say that in their absence responses to questionnaires do not provide a sufficiently sound basis for classification.

2021550780

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Professor Witorsch made criticisms of the studies similar to those made by Professor Tweedie. For the most part, he referred to criticisms of the studies made by other persons and adopted them. This is understandable in view of the fact that he did not claim to be a specialist epidemiologist.

He questioned the meta-analysis exercises carried out by Professor Wald and the National Research Council because he thought they are based on a number of questionable assumptions, particularly the assumption that spousal smoking is a valid and reliable surrogate index for environmental tobacco smoke exposure.

Professor Witorsch made no mention in his proof of evidence of some matters which epidemiologists think are of great importance in reaching a conclusion whether there is a causal association between passive smoking and lung cancer, e.g. whether environmental tobacco smoke contains carcinogenic substances and whether there is no safe dose for carcinogens. In his opinion, the question whether exposure to environmental tobacco smoke is associated with an increased risk of lung cancer remains unresolved.

(l) Professor Huber

Professor Gary Huber has been Professor of Medicine in the Department of Medicine at the University of Texas Health Center since 1985. He has been associated with research, teaching, diagnosis and treatment in the field of pulmonary medicine since 1962. He has been interested in and associated with research into smoking, tobacco smoke and health since 1972 when he became

2021550781

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Director of the Smoking and Health Research Program at the Harvard Medical School, Boston. This program was initiated jointly by the Harvard Medical School and by the major cigarette manufacturers in the United States, with the intent of developing a multi-disciplinary evaluation of the potential health effects of tobacco smoke.

Professor Huber is of the view that the statement made in the advertisement accurately describes the state of the evidence both as at July 1986 and at the present time. He thinks a major difficulty in studying the health effects of environmental tobacco smoke on non-smokers is that non-smokers are exposed to a mixture which is both qualitatively and quantitatively different from that to which active smokers are exposed. He also thinks it is not scientifically appropriate, in the present state of knowledge, to transpose theories concerned with active smoking and health into the field of health issues related to environmental tobacco smoke.

Professor Huber said that although different researchers have reported different levels of nicotine in the atmosphere of places in which smoking occurs, all of the levels reported are low and the majority of reported data indicates that, overall, tobacco smoke contributes very little to indoor environmental pollution. This is a judgment which appears to me to be inconsistent with common experience of some indoor environments.

He said that the constituent chemical components in environmental tobacco smoke include benzo(a)pyrene and other constituents which are found in

2021550782

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

minute quantities in mainstream smoke and in even smaller quantities in environmental tobacco smoke. These are hydrocarbons and can, when applied at high concentrations in condensate form, produce tumours. In his opinion, it has not been demonstrated and it is highly improbable that they present a risk of cancer in humans in the concentrations at which they are found in environmental tobacco smoke.

Professor Huber's evidence related mostly to relationships between environmental tobacco smoke and cardiovascular diseases, acute pulmonary effects, chronic pulmonary effects in adults and children, and asthma. He did not claim to have any special expertise in cancer epidemiology.

He agreed (T.3724) that there are chemicals, such as vinyl chloride, that exist both in mainstream smoke and sidestream smoke and that vinyl chloride had been shown to be carcinogenic in humans. He would not agree, however, that a passive smoker who inhales environmental tobacco smoke may inhale smoke which contains vinyl chloride. He said that some things cannot be detected in environmental tobacco smoke that can be measured in sidestream smoke. He does not know whether vinyl chloride had been detected in environmental tobacco smoke or not. He agreed that it was possible that a small child being nursed by a woman smoking a cigarette might inhale a molecule of vinyl chloride.

When asked whether it is generally accepted that a safe threshold is unlikely to exist for most carcinogens, Professor Huber said that he did not know the

2021550783

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

exact answer to the question. When pressed with the question: "Do you agree that it is unlikely that there is a threshold of low dose exposure to carcinogens below which there is no increase in risk?", he answered: "I would think that there would be a threshold below which the risk is so small that it could not be measured." He agreed in cross-examination that in an article which was published in January 1990 and of which he was the co-author, the following statements appeared:

> *"As summarized by the Surgeon General there is little disagreement that active smoking is associated with an increased risk for the development of lung cancer, with a causal and probable dose response relationship between tobacco smoking and the development of lung cancer."*

> *"Furthermore there does not seem to be any safe threshold for an absolute lower limit of tobacco smoking and the occurrence of lung cancer."*

> *"Depending on the extent of exposure the non-smoker may be exposed to clearly quantitatively lesser amounts of smoke but for some components qualitative exposure of the non smoker may differ little from the active smoker."*

With respect to the last mentioned passage he said he had since expanded his reading significantly and that, at the time he wrote the article, it was the best information he had. He also said that if he were to write the paper again, he would write it differently. I am bound to say that I found some of his answers unsatisfactory, as he did not persuade me that any significant body of scientific material had come to his notice since the paper was written.

Dr Huber claimed that the abovementioned statements had been taken out of context, and in this respect the following excerpt from his evidence is relevant:

2021550784

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

"MR FRANCEY: You complain, doctor, that the two sentences I read to you about threshold and similarity of the quality of smoke that non smokers are exposed to and smokers are exposed to were taken out of context. Can I ask you this then, that in writing that article by way of summary in relation to lung cancer you were of the view last year that some of the existing data show a positive association between passive smoking and lung cancer, although these data do not always necessarily meet strict criteria of causality in this association but considering the large number of persons exposed to passive smoking, even the most minimal potential association for the development of lung cancer in non smokers cannot, however, be ignored?---I would agree with that.

And you would agree with it now?---Yes."

(T.3777)

I did not find Professor Huber a satisfactory witness in all respects. I thought, with all respect to him, that he was sometimes evasive in his answers. That this is so appears, I think, from the following passage in his evidence:

"HIS HONOUR: ... In your opinion, does active smoking cause cancer in some smokers?---In a susceptible group within the smoking population.

No, leaving that aside. If I just ... asked you the question whether in your opinion, does active smoking cause lung cancer in some active smokers, what would your answer be?---My answer would be the same. My answer would be that there are associations and that there are a variety of complex aspects to that question. I am not trying to evade the question. I am trying to say it is a very complex issue and that people who smoke develop lung cancer.

Would this be your answer and do not assent to it if it is not right, would your answer be there is a strong, perhaps very strong association between active smoking and the incidence of lung cancer ... (but) I cannot say that there is a causal relationship between the two?---There certainly is a strong association. I agree with that. I do not understand the nature of the potential causal relationship. I do not know what it is in tobacco smoke that might cause cancer in humans. I know that there are 40 or 50 carcinogens there that cause tumours in animals. I do not know which, if any of those might be responsible for the induction of cancer in humans. I do not know the mechanism by which that occurs. So I am left with a strong association between cigarette smoking and the development of cancer in some individuals and that is a strong association and the mechanisms and the details of which have defied science to this point. Does that answer your question?"

2021550785

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

I think Professor Huber is excessively cautious in drawing conclusions from available data. Of all the witnesses called by the respondent, I found him the least impressive.

(m) Dr Malmfors

Dr Sven Malmfors is an independent consultant in toxicology and risk assessment. He resides in Sweden. He was, for a time, an Assistant Professor in the Department of Histology at the Karolinska Institute in Stockholm. Between 1972 and 1980 he was the head of the toxicology laboratory of a large pharmaceutical company. He left that position in 1980 to go into private practice as an independent consultant. He has worked part-time in the teaching of toxicology and the training of graduates in the science of toxicology. He is a past President of the Swedish Society of Toxicology.

In his capacity as a consultant, Dr Malmfors has spoken at seminars on behalf of the tobacco industry. Such seminars have been concerned with exposure to environmental tobacco smoke.

Dr Malmfors is of the opinion that the statement made in the advertisement was accurate at the time it was published and is still accurate. He said that a toxicological evaluation to determine the toxicity of a given chemical to humans requires the accumulation of data which may come from experimentation or epidemiology. Such experimentation may involve testing a biological system under artificial conditions in a laboratory, or experiments with animals or humans. He said

2021550786

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

if there are no experimental data other than epidemiological data, this is usually not sufficient from a toxicological point of view to establish a cause/effect relationship.

He drew attention to what he said were the qualitative and quantitative differences between mainstream and environmental tobacco smoke. He said that unless particular chemicals, either alone or in the same combination, can be shown to be present in both mainstream and environmental tobacco smoke, it is not scientifically proper to extrapolate from mainstream smoke components to environmental tobacco smoke components or to use the former to found a reasoning process based on analogy. He thinks that data derived from experiments concerning the effect of mainstream smoke on animals is not relevant to the question whether passive smoking causes cancer in humans. The results of such experiments cannot, in his opinion, be extrapolated to exposure to environmental tobacco smoke.

It seems to me that Dr Malmfors' requirements for the establishment of scientific truth are almost unattainable. Some idea of the degree of proof which he would require before being persuaded of a scientifically proved cause/effect relationship between environmental tobacco smoke and lung cancer may be gained from the opinions which he expressed as to the proof (or absence of it) of a cause/effect relationship between active smoking and lung cancer. His evidence included the following:

> *"HIS HONOUR: Would you agree that tobacco smoke contains several agents which are cancer initiating and mutagenic?---Depends on under which circumstances. There are chemicals in mainstream smoke which under certain conditions initiate tumours and that is true.*

2021550787

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Well under conditions which obtain when a human inhales the smoke?---No, I consider those conditions different from those conditions where there are proof of [carcinogenicity] for those ...

I am not talking about ETS. I am talking about the active smoker?---Yes.

Is the smoke which he inhales, smoke which contains several agents which are cancer initiating and mutagenic?---Yes, but the problem is that they are not cancer inducing and mutagenic everywhere under every condition. There are certain conditions which have to be fulfilled before that, in effect, can occur.

Is it not your belief that those conditions are very often fulfilled and that that leads to what is said to be an increased incidence of lung cancer in active smokers?---I do not know which those conditions are so I cannot comment on that."

(T.2270)

He said (T.2259) he was unable to point to any evidence that showed there was a safe dose for any of the carcinogenic substances in tobacco smoke. He agreed that epidemiological studies have reported an association between active smoking and the incidence of lung cancer in smokers but he said, quite positively, that he did not accept that direct smoking causes lung cancer. He conceded that it was possible that there may be important toxicological data obtained from research in connection with active smoking that might throw light on the effect of environmental tobacco smoke, but that he had not studied it. I am bound to say that I found this concession surprising coming from a scientist of his calibre who is so closely interested in the effects of environmental tobacco smoke that he addresses seminars on the subject on behalf of the tobacco industry. I think it reflects a very narrow scientific approach and a reluctance to consider all available data which might contribute to an understanding of the effects, if any, of passive smoking.

2021550788

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

(n) Professor Clayton

Professor John Clayton is Professor Emeritus of Pharmacology and Toxicology at the University of Arizona. He held the positions of Professor of Pharmacology and Toxicology and Professor of Microbiology and Medical Immunology at the University from 1974 to 1989.

Professor Clayton referred to the quantitative and qualitative differences which he thinks distinguish mainstream smoke from environmental tobacco smoke. Based on toxicological data from animal inhalation experiments Professor Clayton's opinion is that the statement in the advertisement was accurate at the time it was published and is still accurate.

He thinks that in order to evaluate a hypothesis as to whether or not environmental tobacco smoke causes chronic disease such as lung cancer in humans, scientists must consider two major types of data: epidemiological and toxicological. In his opinion, epidemiology alone is not sufficient to establish a cause and effect relationship. He thinks that well designed and well conducted animal experiments are required in addition to epidemiological data before it can be scientifically concluded that a particular agent causes a specific chronic disease. He knows of no animal inhalation experiments investigating the effects of environmental tobacco smoke as at 1 July 1986. In the absence of such studies he thinks there was no pertinent toxicological evidence at that time and that therefore, it had not been proved scientifically that environmental tobacco smoke caused chronic disease in non-smokers.

2021550789

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Professor Clayton said that there had been two animal experiments since July 1986 in which attempts had been made to measure the effects of environmental tobacco smoke on hamsters. One experiment revealed pulmonary changes in the hamsters, but of a kind which could have been expected to occur under similar exposure to other agents, e.g. dust. The investigators who carried out the other experiment reported that overall there was no marked increase in tumour incidence in animals exposed to either mainstream smoke or sidestream smoke over the normal lifespan of a hamster.

With reference to three studies referred to by Professor Stewart in his evidence, (Harris et al, Bernfeld et al and Dalbey et al) Professor Clayton said they were all studies concerned to simulate active smoking by exposure of mice, rats or hamsters to mainstream smoke, not environmental tobacco smoke. In any event, he thought there were other problems about the experiments, including that the concentrations of smoke used were very high and quite different from human exposure to environmental tobacco smoke. As to the theory that one molecule of a suspected carcinogen may initiate a carcinogenic process, the professor said there was no way to prove or disprove this theory.

Professor Clayton is of the opinion that toxicology has not provided any proof that mainstream smoke causes lung cancer in active smokers. As he said: "The toxicologist would say there is no demonstration that cigarette smoke inhalation causes lung cancer in humans." (T.2941). He accepted that some substances found in tobacco smoke, e.g. vinyl chloride and napthylamine are listed in the IARC report

2021550790

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

(Appendix Z at pp.389-94) as being chemicals in respect of which there is sufficient evidence that they are carcinogenic to both animals and humans. But as I understood his evidence, he was not prepared to concede that this was indeed the case.

The respondent tendered as part of its case Chapter 4 of the 1982 report of the United States Surgeon General on the health consequences of smoking in which the statement is prominently made that - "Cigarette smoking is the major single cause of cancer mortality in the United States."

Professor Clayton's views do not rest easily with this statement.

(o) Mr Leslie

Mr George Leslie is an independent toxicologist and pharmacologist. Between 1974 and 1987 he was head of the Toxicology and Pathology Department of Smith Kline and French where he worked on many projects of a toxicological nature. He has been a full time consultant in toxicology since 1987. He has lectured to students at a number of academic institutions, including London University and is an examiner of the candidates for the degree of Doctor of Philosophy in Pharmacology and Toxicology at the University of Wales. He has written many scientific papers.

Mr Leslie expressed the opinion that the statement made in the advertisement was accurate as at 1986 with respect to possible health effects on the embryo or foetus in a woman exposed to environmental tobacco smoke. I have had regard to what Mr Leslie said in his evidence regarding matters such as the nature of

2021550791

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

scientific proof and the distinction between proof of an association and proof of a cause and effect relationship. The bulk of Mr Leslie's evidence relates to matters other than the association, if any, between passive smoking and cancer in non-smokers and I shall not refer to it in the present context.

(p) Professor Warren

Professor Warren is professor of Pathology at the University of New South Wales and has impressive qualifications as a pathologist. He described the histologic, cytologic and clinical techniques for diagnosing cancer of the lung and some of the limitations of these techniques. His evidence was essentially non-controversial. The limitations of which he spoke were recognised by the applicant's witnesses. I do not think they diminish the weight which I should give to their evidence and to the findings referred to in the primary articles.

(v) Comments on the epidemiological evidence

The respondent's witnesses, particularly Professor Tweedie and Dr Layard, criticised the methodology and quality of all the epidemiological studies upon which the applicant's witnesses relied. To a greater or lesser extent, the studies were said to be flawed because of a number of factors. These factors included reliability of the diagnoses of lung cancer, the adequacy of data provided by surrogate respondents, the representativeness of data, possible sources of bias and misclassification, the unreliability of using spousal smoking habits as an indicator of

2021550792

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

exposure to environmental tobacco smoke, and failure to account for confounding factors.

I think it is fair to say that the applicant's witnesses conceded, to a limited extent, that the results in some of the studies may have been affected by some of these factors, albeit not to the extent of making them unreliable. In their opinion, it was the pattern which emerged from the studies which was important. This opinion is reflected in Chapter 7 of the NH&MRC report where the following statement is made:

> *"In reviewing the literature on passive smoking and lung cancer, it is important to include an overall assessment of the directionality and coherence of the findings from the various individual studies. Given the methodological impediments to making a conclusive finding in any one epidemiological study, then it is important to examine the pattern of findings. If, despite limitations and flaws in individual studies, substantial consistency emerges - as is the case for the reported evidence on passive smoking and lung cancer - then the prudent public health response must be to infer that a real effect is likely."*

I have referred above to statements to the same effect by some of the applicant's witnesses.

Counsel for the respondent submitted that Dr McMichael had, in effect, conceded that there was no demonstrated causal link between passive smoking and lung cancer in a paper he submitted to the National Health & Medical Research Council Carcinogenic Substances Committee in March 1983 (Ex.104). In that report, after a detailed discussion of the studies by Hirayama, Trichopoulos (1981 study only) and Garfinkel (1981 study only), he said that while the available epidemiological evidence suggested that passive smoking may increase the risk of lung cancer, the

2021550793

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

limitations in data and study design did not then allow a judgment on causality. But this paper was produced at a very early stage in the on-going investigation into the possible health hazard from passive smoking.

The intrinsic difficulties in appraising epidemiological studies of passive smoking and health are recognised in the scientific literature. Many of the limitations and criticisms of the studies referred to in the primary articles are dealt with in considerable detail in Chapter 2 of the Surgeon General's report. The Surgeon General's comments appear to me to be valid and I adopt them as part of these reasons. No useful purpose would be served by repeating them.

However, there are a few general comments I should make about the epidemiological evidence. In the first place, I think that more reliance can be placed upon non-statistically significant results than the respondent's witnesses were prepared to concede. I agree with Sir Richard Doll's view that statistical significance is "a guide to thought" rather than an absolute standard. If a positive relative risk is statistically insignificant because, say, the lower confidence limit is marginally below 1, I do not think that it should be rejected from consideration for that reason alone. In such a situation, lack of statistical significance calls for the exercise of caution in evaluating the study, but that is not to say that it disqualifies the study from consideration.

On a related matter, I think that non-statistically significant data which, considered in isolation from other data, may be of little value in forming an

2021550794

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

epidemiological judgment, may well be valuable aids to judgment if they form part of a pattern of positive findings.

I agree that spousal smoking is an imprecise measure of total exposure to passive smoke because it accounts for only one of what may be many possible sources of tobacco smoke exposure. But with all its imprecision, it seems to me to afford a reasonable basis for measuring exposure.

The applicant's and the respondent's witnesses were generally agreed that what are known as the Bradford Hill criteria are standard criteria for evaluating epidemiological studies. However, the respondent's witnesses placed more store on the observance of all the criteria than did the applicant's witnesses. For instance, Dr McMichael thought the criteria should be applied only subject to a caveat. He said (T.1238):

> *"Well, it is a general caveat that, whilst those are well-recognised as useful and often important criteria in the drawing of judgments about causal inference, they are not and should not be seen as pre-requisites. In other words the drawing of causal inferences can quite reasonably proceed and often does in the presence of just several of those criteria."*

It is this approach which appears to me to explain the differing views of the applicant's and the respondent's witnesses as to the evidentiary value of the studies referred to in the primary articles. I prefer the approach taken by the applicant's witnesses to that taken by the respondent's witnesses.

2021550795

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

As to misclassification, I take the view that although the risk of it occurring is always present, the respondent's witnesses have tended to exaggerate its significance and not to have regard to the fact that it is often random in its distribution.

I think the respondent's witnesses tended to underestimate the biological plausibility of a causal link between passive smoking and lung cancer. I agree with Professor Trichopoulos' evidence that:

> *"It is one thing to find strong statistical significance which comes out of the blue and it is quite different to find statistical significance [in] something which is suspected on the [basis] of biological grounds ...."*
>
> (T.4030)

Without wishing to derogate from the expertise of Professor Tweedie and Dr Layard as statisticians, I think their assessment of the value of the studies referred to in the primary articles tended to be over-technical. I have formed the opinion that the evaluations of the studies by the epidemiologists called by the applicant are to be preferred to the evaluations of them made by Professor Tweedie and Dr Layard.

It emerged from time to time in the evidence that a statistician is less likely to find evidence of proof in an epidemiological study than is an epidemiologist. Because of Dr Layard's close association with the tobacco industry, it seems highly unlikely that he is unaware of the epidemiological studies as to the existence of a causal link between active smoking and lung cancer. As I have already noted, Chapter 4 of the 1982 report of the Surgeon General (which was tendered by the

2021550796

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

respondent) contains a most positive statement that active smoking causes cancer in smokers. Yet when Dr Layard was asked whether he had formed an opinion on the question whether a causal relationship had been established between active smoking and any form of disease, he said (T.2720) that he had not formed an opinion on that subject. When pressed why that was so he said: "I can only say that I do not feel that my knowledge of biological matters is sufficient for me to arrive at an informed conclusion on that subject."

I also think that Dr Witorsch and Professor Huber took an over-technical approach to the epidemiological evidence and were hypercritical of it.

(vi) Is there more than a little evidence that cigarette smoke causes cancer in non-smokers?

In my opinion, the applicant has established that, in relation to the disease of cancer, it was misleading and deceptive to state on 1 July 1986 that there was then little evidence that cigarette smoke causes disease in non-smokers. So far from there then being little evidence that cigarette smoke caused lung cancer in non-smokers, there was much evidence to that effect. That was the situation, even if only the data referred to in the primary articles is regarded as evidence for the purposes of the advertisement. Measuring that evidence by any standard, it cannot be fairly described as "little".

Unaided by the opinions of the experts who were called, I would have concluded that it cannot be described as "little". The opinions of the experts called in

2021550797

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

the applicant's case confirm my conclusion. I much prefer the opinions of the applicant's witnesses on this matter. The evidence of a link between passive smoking and lung cancer comes from epidemiological studies supported by strong biological plausibility. The epidemiologists called by the applicant were most impressive witnesses. Their opinions are shared by many other distinguished epidemiologists who took part in the compilation of the major reviews.

The respondent did not call one witness whose primary expertise was in the field of epidemiology. I do not overlook the fact that Professor Huber and Professor Witorsch have some experience in the field, nor that Professor Tweedie and Dr Layard are experienced statisticians. Nor is it a matter merely of counting heads. Rather it is a matter of judging, as best I can, which opinions are entitled to the most weight. I have no hesitation in preferring the opinions expressed by the applicant's witnesses.

I have reached the conclusion that the opinions of the experts called by the applicant are to be preferred to the opinions expressed by the experts called by the respondent. I think the applicant's witnesses had more experience in some matters upon which they disagreed with the respondent's witnesses. In particular, on questions concerning the carcinogenic qualities of tobacco smoke and the existence or otherwise of a safe level of exposure to carcinogens I found the evidence of Professor Stewart very persuasive and I prefer it to the respondent's evidence on the same matters.

2021550798

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

As I have noted, the applicant's witnesses said that the statement that there is little evidence that cigarette smoke causes cancer in non-smokers is incorrect. I did not understand the respondent's counsel to submit that evidence of this kind was inadmissible. However, it was submitted that the statements by the applicant's witnesses as to their own opinions on the question whether cigarette smoke causes disease in non-smokers is not evidence in the sense in which that word is used in the advertisement. It was submitted that any probative value attaching to the findings referred to in the primary articles was not increased by the applicant's experts expressing their concurrence with them. I think there is some substance in this submission, but I do not think it advances the respondent's case. The experts were entitled to explain the contents of the primary articles and to depose as to the strengths and weaknesses of the studies referred to in them. If, after examination of a primary article, it is seen to disclose some evidence of a causal relationship between passive smoking and lung cancer it is hardly necessary for an expert to express his opinion that it does so.

Of course, if it is relevant to have regard to the state of the evidence after 1 July 1986 and to major reviews as well as primary articles, the applicant's case becomes even stronger. As I have said earlier in these reasons, I think that the applicant is not confined to the state of the evidence as at 1 July 1986 and I also think that the major reviews are "evidence" as that word is used in the advertisement.

On the question of the relevance of articles published after 1 July 1986, I should make special reference to the Wald article on meta-analysis. Although the

2021550799

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

article was published after 1 July 1986, the studies which Professor Wald and his co-authors analysed were all published before that date. The meta-analysis which they carried out could as easily have been carried out on 1 July 1986. What the article did was to show the strength of the evidence as it existed at 1 July 1986, not as at the date of publication of the article. Hence, I think regard can be had to the article for the purpose of assessing whether it was misleading or deceptive to say, as at 1 July 1986, that the evidence which then existed was "little".

Since I am of the opinion that on no view of the meaning of the word "little" can the evidence that passive smoking causes disease in non-smokers be so described, there is no need to attach a precise meaning to the word. The essential message which the advertisement, as a whole, attempts to convey to the reader is that cigarette smoke may be annoying to some non-smokers but that (as stated in the penultimate paragraph) " ... annoyance is neither a governmental nor a medical problem". In substance, what the reader is told is that inhalation of cigarette smoke by non-smokers may be annoying to them but it is not a health problem. Having regard to the totality of the advertisement, the reference to "little evidence" seems to be a reference to evidence which is so inconsequential as not to support a reasonable apprehension that passive smoking may give rise to a medical or health problem.

It was submitted on behalf of the respondent that the evidence called by the applicant was not evidence that cigarette smoke causes disease in non-smokers. The evidence, so it was submitted, was no more than evidence of an association between cigarette smoke and disease. I am unable to accept that evidence of an

2021550800

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

association between passive smoking and lung cancer cannot be regarded as some evidence of a causal relationship between the two.

Nor do I accept the respondent's related submission that epidemiological evidence alone cannot establish a cause and effect relationship. The submission would be valid only if the standard of proof required to establish such a relationship is set at a virtually unattainable level.

(vii) Is there scientific proof that cigarette smoke causes cancer in non-smokers?

I have not so far considered whether the statement is erroneous in so far as it asserts that there is nothing which proves scientifically that cigarette smoke causes disease in non-smokers. As I have observed, I think that in the context of the advertisement the words "nothing which proves scientifically that cigarette smoke causes disease in non-smokers" mean "nothing which affords compelling or convincing evidence that cigarette smoke causes disease in non-smokers". Reading the statement in this way, I have come to the conclusion that it is erroneous.

The conclusion that cigarette smoke causes lung cancer in non-smokers cannot be drawn from any one epidemiological study or piece of evidence. But I think it can be drawn from the totality of the available data and by valid reasoning from it. A summary of the reasons which lead me to this conclusion is contained in the statement with which Professor Wald concluded his proof of evidence. I agree with what he there said, which was as follows:

2021550801

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

> *"In our 1986 paper we concluded that breathing other people's tobacco smoke was a cause of lung cancer and our conclusion rested on several sources of evidence, not only the statistically significant association between lung cancer and exposure to environmental tobacco smoke. It also rested on other evidence, including the fact that carcinogens in tobacco smoke are released into the air and that tobacco smoke is breathed into the lungs by non-smokers. Non-smokers who are exposed to environmental tobacco smoke absorb tobacco products into their blood and tissues, and their urine contains chemicals that are mutagenic, that is chemicals that can induce change in the genetic material in a manner that is thought to be fundamental to the initiation of cancer. It is known that active smoking causes lung cancer, a strong effect in which the risk of lung cancer is some 14 times that in non-smokers. It is the accepted scientific view that exposure to carcinogens does not have a threshold below which there is no effect and therefore one would expect that non-smokers who inhale environmental tobacco smoke would have at least some increased risk of lung cancer. The conclusion that the excess risk is of the order of 30-50% is plausible in the light of the much higher risk of lung cancer due to active smoking. Given all the evidence I believe that the conclusion that breathing other people's smoke is a cause of lung cancer is scientifically sound."*
>
> (Ex.SS, pp.15-16)

It is obvious that Professor Wald's views that environmental tobacco smoke contains substances which are carcinogenic to humans and that there is no threshold level of exposure to carcinogens below which they cannot and do not cause cancer in humans, form an important part in his overall reasoning.

The expert witnesses called by the applicant all accepted the validity of these views. They are also shared by numerous distinguished authors of many of the primary articles and major reviews. Those few scientists (and they mostly have a professional association with the tobacco industry) who do not share their views claim that their validity has not been established. They do not go so far as to assert that the conclusions are invalid.

2021550802

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Once it is accepted:

(a) that passive smoking involves inhalation of environmental tobacco smoke which contains carcinogens;

(b) that there is no safe threshold level of exposure to carcinogens:

(c) that some of the studies referred to in the primary articles show a statistically significant association between spousal smoking and lung cancer; and

(d) that meta-analysis of the results in such studies discloses a statistically significant (adjusted) risk ratio of about 1.53 (Wald et al) or 1.42 (NRC report) for non-smokers living with smokers compared with non-smokers not exposed to environmental tobacco smoke;

then my conclusion must be that there is compelling scientific evidence that cigarette smoke causes lung cancer in non-smokers. Although not based upon the findings made by the authors of the major reviews, my conclusion is consistent with those findings.

Counsel for the respondent submitted that such a conclusion cannot be drawn because some of the applicant's witnesses conceded that other scientists may hold a contrary view. I do not accept this submission. I did not understand any of the applicant's witnesses to concede that their opinions were or might be incorrect merely because some hypothetical scientist may hold a contrary opinion.

Moreover, the views held by other scientists may be formed upon the basis even that compelling evidence that passive smoking causes lung cancer does not

2021550803

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

establish proof for the purpose of the statement in the advertisement. Indeed, I have formed the view that the opinions of the respondent's witnesses are difficult to justify except on this basis. An extract from the evidence of Dr Leslie (T.3470-1) illustrates this point:

> *"HIS HONOUR: ... assuming over a period of 50 years in every country of the world an odds ratio of 10 had been established in respect of smokers who smoked two packets of cigarettes a day in relation to risk of cancer but no toxicology or other studies had been undertaken, all you had was there was a stream of consistent statistically significant results of that kind. That would be, what, no evidence that cigarette smoke caused cancer in smokers?*
>
> *WITNESS: Well, it would be no direct evidence. It would be . . .*
>
> *HIS HONOUR: It would point to a relationship?*
>
> *WITNESS: It would make you put the odds against it of there being a causal link as something astronomic but it still would not be proof."*

It was also submitted that there are statements in the NH & MRC report which virtually concede the absence of scientific proof of a causal link between passive smoking and lung cancer. Reference was made particularly to the following statement made on p.33 of the report:

> *"The evidence that passive smoking causes lung cancer is strongly suggestive. It is plausible, moderately consistent, and demonstrates dose-response relationships. However, intrinsic difficulties in accurately classifying individual exposure, and insufficient numbers of study subjects in many studies, preclude a conclusive interpretation of these empirical data when considered in isolation from other corroborative scientific evidence."*

Dr McMichael said that the above passage under-stated the view of many scientists, including himself. More importantly, the passage on p.33 is followed by a reference

2021550804

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

to conclusions contained in the IARC report. After referring to the statement in that report that: "The observations on non-smokers that have been made so far are compatible with either an increased risk from passive smoking or an absence of risk" Dr McMichael and his colleagues conclude the chapter in the NH & MRC report on passive smoking and cancer with the following statement, with which they apparently agree, in the IARC report:

> *"Knowledge of the nature of sidestream and mainstream smoke, of the materials absorbed during 'passive' smoking, and of the quantitative relationships between dose and effect that are commonly observed from exposure to carcinogens, however, leads to the conclusion that passive smoking gives rise to some risk of cancer."*

It is to be noted that this passage in the IARC report is followed by the following statement:

> *"There is sufficient evidence that tobacco smoke is carcinogenic to humans."*

As I have already observed, I regard the reference to "tobacco smoke" as a reference to all kinds of tobacco smoke, including environmental tobacco smoke. In IARC's lexicon, "sufficient evidence" of carcinogenicity indicates that there is a causal relationship between the exposure and human cancer - vide p.24 of the IARC report.

As I understand what is said in these statements in the NH & MRC and IARC reports, the authors of them accept that the epidemiological studies which had been made prior to the making of the reports, taken in isolation from other scientific evidence, did not demonstrate that passive smoking causes lung cancer. But they

2021550805

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

appear to conclude that a consideration of the totality of all the scientific evidence leads to the conclusion that passive smoking gives rise to some risk of cancer, i.e. that some people will suffer from cancer as a result of their passive smoking.

Reliance was also placed by the respondent upon some statements made in Chapter 9 of the NH & MRC report, in particular the following passage:

> *"Council notes that there is mounting epidemiological evidence that passive smoking may increase the risk of occurrence of lung cancer. Despite limitations in the amount of data available, and despite research difficulties in making satisfactory estimations of individual exposure, a consistent pattern of moderately increased risk of lung cancer in passive smokers has emerged. In view of this pattern, of the known and substantial increase in risk of lung cancer in active smokers (and the lack of a threshold dose), and of the documented levels of bodily assimilation of passively-inhaled smoke, it is therefore prudent public health policy to infer an increased risk of lung cancer from passive smoking."*

It was argued that the language used in the latter part of the above statement indicated that the authors of it were not persuaded that there was a proven link between passive smoking and lung cancer. It should be noted that Chapter 9 of the report was not written by the members of the working party, who were the authors of the chapter on passive smoking and cancer. Chapter 9 is the work of the National Health and Medical Research Council itself. Dr McMichael said that the function of the Council is to advise the Australian Government on matters of public health policy and this no doubt explains the language used by the Council. I do not think the language used by the Council should be taken as qualifying the views of the authors of Chapter 7 of the report.

2021550806

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

It was also submitted on behalf of the respondent that the authors of the NRC report did not reach a firm conclusion that passive smoking is a cause of lung cancer. I do not think this is the case. The National Research Council reached the conclusion that the relative risk of cancer incurred by "exposed" non-smokers compared with a truly unexposed non-smoker was 1.42. (This figure compares with Professor Wald's calculated equivalent relative risk of 1.53). The authors of the report then make the following statement (p.242):

> *"We can say, therefore, that while the epidemiologic studies show a consistent and, in total, a highly significant association between lung cancer and ETS exposure of nonsmokers, the excess might, in principle, possibly be explained by bias. However, detailed consideration of the nature and extent of the bias shows that given some reasonable assumptions the bias would be insufficient to explain the whole effect. In fact, there are some types of bias that lead to underestimates of the effect. It must be concluded, therefore, that some, if not all, of the effect reported in spouse studies is causal."*

This statement is made on the basis of the epidemiological studies alone. When regard is had to the generally accepted view that exposure to carcinogens does not have a threshold below which there is no effect, the findings in the NRC report do not stand in the way of the conclusion which I have reached that there is compelling scientific evidence that passive smoking does indeed cause lung cancer.

It follows from what I have written that the statement: "Yet there is little evidence and nothing proves scientifically that cigarette smoke causes disease in non-smokers" was erroneous when it was first made on 1 July 1986 and remains so.

2021550807

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

8. Respiratory Disease Young in Children

It is apparent from a consideration of the primary articles, the major reviews, and the oral evidence given by the applicant's and the respondent's witnesses that the applicant's case that cigarette smoke causes respiratory disease in non-smokers is at its strongest with respect to respiratory disease in children under the age of 12 months. For that reason I think it is unnecessary for the purpose of deciding the issues which arise in the present case to examine in detail the evidence as to the association between passive smoking and respiratory effects and pulmonary function in older children or in adults. If the applicant cannot, in respect of this part of its case, succeed in respect of children in the first year of life, it cannot succeed at all. I therefore do not propose to refer in any detail to the evidence as to the effect of passive smoking on older children or adults.

Before referring to the oral evidence in this part of the case I shall set out some of the statements made in the primary articles and the major reviews upon which the applicant places reliance.

.../141

2021550808

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

(f) The primary articles

(a) Harlap and Davies - Infant admissions to hospital and maternal smoking.

This article appeared in The Lancet in 1974. The authors of the article were from the Department of Medical Ecology at the Hebrew University, Jerusalem. The following summary of the study appears in the article:

> *"Admissions to hospital during the first year of life were recorded in a prospective study of 10,672 infants whose mothers' smoking habits were known. Infants with major congenital malformations, and those dying before their first birthday, were excluded. The infants of mothers who smoked had significantly more admissions for bronchitis or pneumonia, especially in the winter, and more injuries. They were also admitted more frequently, though not significantly so, for upper-respiratory-tract infections, gastroenteritis, childhood infectious diseases, and other diagnoses. The excess of bronchitis and pneumonia in the group exposed to smoke increased with increasing number of cigarettes smoked by the mother. It occurred within subgroups of birth-weight, social class and birth order. It was seen mainly in infants aged 6-9 months, while at older and younger ages there was no significant effect of maternal smoking. The findings support the hypothesis that atmospheric pollution with tobacco smoke endangers the health of non-smokers."*

There was a study population of 10,672. At the time of the interviews, 9.2% of the mothers were smokers and 7.4% had given up smoking earlier. The admission rate (per 100 infants) for bronchitis and pneumonia was 9.5 for children of non-smokers and 13.1 for children of smokers. The equivalent figures for admissions for upper respiratory tract infections were 4.8 and 5.3 respectively, but these last-mentioned figures were not statistically significant. The article contains a table giving admission rates (per 100 infants) by diagnosis in relation to maternal smoking and the number of cigarettes smoked daily. The table is as follows:

2021550809

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

TABLE II - ADMISSION-RATES (PER 100 INFANTS) BY DIAGNOSIS, MATERNAL SMOKING AND NUMBER OF CIGARETTES SMOKED DAILY

Diagnosis	Non-smokers		Smokers			Total (10,672)
	Never smoked (8900)	Former smokers (786)	Cigarettes per day			
			1-10 (747)	11-20 (747)	21 + (60)	
Bronchitis and pneumonia	9.6	7.8	10.8	16.2	31.7	9.8
All other	15.5	15.1	16.4	17.3	23.3	15.6
Total	25.1	22.9	27.2	33.5	55.0	25.4

Differences among three categories of smokers: for bronchitis and pneumonia, $P < 0.001$, for other diagnoses, not significant.

The authors included the following observations in their study:

"Infants born to smokers were in hospital for an average of 384 days per 100 infants before their first birthday, 151 of them for bronchitis or pneumonia. These rates were 334 and 114, respectively, for the infants of non-smokers. However, there were no significant differences between the groups, exposed or not exposed to smoke, in average duration of each type of admission episode.

Admissions for bronchitis or pneumonia increased in frequency with increasing number of cigarettes smoked by the mother (table II). There were no significant increases for any of the other diagnoses measured separately. Infants of mothers who had given up smoking had fewer admissions than those whose mothers had never smoked. This difference, which can be explained by the higher standard-of-living of those who gave up smoking, is not, however, statistically significant for any single diagnostic category. Infants born to former smokers spent fewer days in hospital in the first year of life (231 per 100 infants, 79 of them for bronchitis or pneumonia), and their admission episodes tended to be shorter for each diagnosis.

2021550810

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Women who smoke gave birth to smaller infants, and birth-weight is an important predictor of admission to hospital in West Jerusalem. Admissions for bronchitis or pneumonia are more frequent in infants who are smaller or larger than average at birth; while for other diagnoses, increasing birth-weight predicts a decreasing probability of going to hospital. Table III shows that the excess of admissions for bronchitis or pneumonia in the passively smoking infants could not be wholly attributed to lower birth-weights, rates being higher than in the infants of non-smokers for all three birth-weight groups."

...

"The excess risk associated with maternal smoking was not uniform throughout the first year of life ... In the first 5 months of life there were no significant differences between infants born to smokers or non-smokers in rates of admissions for bronchitis or pneumonia. Between the ages of 6 and 9 months, on the other hand, there were greatly increased rates of lower respiratory disease in the group exposed to smoke, both in the summer and in the winter. Toward the first birthday, differences between the two groups again disappeared."

In their discussion of the findings, the authors state:

"This study relies on information on maternal smoking which was collected antenatally. It is not known how closely smoking in early pregnancy or mid-pregnancy correlates with habits after the birth and in the baby's first year, but it seems reasonable to assume that for most mothers, smoking characteristics would have remained the same. However there would inevitably have been some smoking mothers who subsequently gave up the habit, and others, especially former smokers, who took it up later. As a result, this study tends to underestimate true differences between infants of smokers and non-smokers, rather than the opposite."

(b) Colley et al. - Influence of passive smoking and parental phlegm on pneumonia and bronchitis in early childhood.

The authors were from the Department of Medical Statistics and Epidemiology at the London School of Hygiene and Tropical Medicine and from the

2021550811

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Department of Community Medicine at St Thomas's Hospital Medical School, London.

This article appeared in The Lancet in November 1974. The following summary of the study appears in the article:

> *"The incidence of pneumonia and bronchitis has been studied in 2205 infants over the first five years of life. In the same period their parents' smoking habits and respiratory symptoms were recorded annually. The incidence of pneumonia and bronchitis in the first year of life was associated with parents' smoking habits; incidence was lowest where both parents were non-smokers, highest where both smoked, and lay between these two levels where only one parent smoked. Over the age of one year the association was not consistent. When parents' respiratory symptoms were also studied a close association was found with the incidence of pneumonia and bronchitis in the child; this was independent of parents' smoking habits and was an almost consistent finding throughout the first five years of life. In the first year of life exposure to cigarette smoke generated when parents smoked doubled the risk for the infant of an attack of pneumonia or bronchitis."*

This study was conducted in Harrow, north-west of London, between 1963 and 1969 and involved all families living in six of the wards of the borough of Harrow who had an infant born in the period from July 1, 1963 to June 30, 1965. 2205 families were included in the study. After exclusions for some cases, such as multiple births, there were 2149 infants eligible for study. It was a longitudinal study conducted over five years. The authors describe the methodology of their study in considerable detail. Some of the results of the study are stated to be as follows:

> *"The annual incidence per 100 children of pneumonia and bronchitis is given in table II by parents' smoking habit. Parents have been classified into one of four groups: (1) both parents non-smokers; (2) one parent smoker, the other non-smoker; (3) both parents smokers; (4) both parents*

2021550812

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

ex-smokers, or one an ex-smoker, or parents who changed their smoking habits during the study. The incidence of pneumonia and bronchitis in the infant shows a gradient by parents' smoking habit in the first year of life. Incidence is lowest in infants with both parents non-smokers, highest where both parents smoke, and lies between these values where one parent smokes. This is a statistically significant gradient (P <0.0005). In subsequent years there is no such clear gradient.

In table III parents have been classified both by their smoking habits and by their response to the question 'Did you usually bring up any phlegm from your chest first thing in the morning in the last winter?' In all categories except one, the incidence within a smoking category is higher among children where one or both parents have winter morning phlegm than in children whose parents are both free of this symptom. Some of the incidence-rates in the children - in particular those whose parents are both non-smokers and who have winter morning phlegm - are based upon small numbers and therefore may not be wholly reliable. On the other hand, the incidence-rates in children where neither parent has symptoms, whether they smoke or not, are based upon substantial numbers. In them in the first year of life a consistent gradient is seen in the incidence of pneumonia and bronchitis in the children in relation to the parents' smoking habits. The rates are lowest in children of non-smoking parents and highest where both parents smoke. In children over the age of a year there is, however, no consistent gradient.

Exposure of the child to cigarette smoke may be more precisely estimated from the total daily cigarette consumption of both parents. In table IV the incidence of pneumonia and bronchitis is given for parent pairs smoking between them 1-14, 15-24, and 25 or more cigarettes per day, by the presence of winter morning phlegm. A clear gradient of increasing incidence is seen in the first year of life that is independent of the presence of winter morning phlegm and is of the same size as that in table III. In the second year and thereafter the pattern is not consistent and thus does not suggest an effect of exposure to tobacco smoke at ages over one year."

.../146

2021550813

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Tables II, III and IV are reproduced below:

TABLE II - PNEUMONIA AND BRONCHITIS BY PARENTS' SMOKING HABITS

Year of follow-up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis				
	Both non-smokers	One smoker	Both smokers	Both ex-smokers or one ex-smoker or smoking habit changed	All
1	7.8 (372)	11.4 (552)	17.6 (478)	9.2 (675)	11.5 (2077)
2	6.1 (338)	9.3 (494)	8.9 (434)	7.4 (758)	8.3 (2048)
3	7.0 (342)	10.2 (480)	9.1 (396)	8.9 (834)	8.9 (2052)
4	6.4 (323)	8.3 (408)	9.0 (357)	8.4 (888)	8.1 (1976)
5	7.3 (319)	6.7 (374)	6.5 (340)	6.6 (954)	6.7 (1989)

TABLE III - PNEUMONIA AND BRONCHITIS IN THE FIRST FIVE YEARS OF LIFE BY PARENTS' SMOKING HABIT AND MORNING PHLEGM

Year of follow up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
	Both non-smokers		One smoker		Both smokers		Both ex-smokers or one ex-smoker or smoking habit changed		All	
	N	O/B	N	O/B	N	O/B	N	O/B	N	O/B
1	7.6 (343)	10.3 (29)	10.4 (404)	14.8 (128)	13.3 (259)	25.0 (139)	8.3 (548)	13.2 (129)	10.1 (1682)	16.7 (425)
2	6.1 (322)	6.5 (34)	7.1 (365)	15.8 (129)	8.7 (286)	9.2 (152)	4.5 (599)	10.7 (159)	7.4 (1572)	11.5 (474)
3	6.9 (305)	8.1 (37)	10.5 (350)	9.4 (107)	7.0 (342)	11.0 (154)	8.2 (664)	11.4 (175)	8.4 (1561)	10.4 (471)
4	8.0 (287)	11.1 (36)	7.3 (368)	10.0 (102)	7.6 (326)	11.6 (121)	8.2 (688)	9.1 (189)	7.9 (1524)	10.3 (446)
5	6.7 (285)	14.7 (34)	5.6 (367)	9.4 (107)	5.9 (288)	10.6 (132)	6.4 (737)	7.3 (239)	5.9 (1497)	9.1 (492)

N = neither with winter morning phlegm. O/B = one or both with winter morning phlegm

2021550814

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

TABLE IV - PNEUMONIA AND BRONCHITIS BY NUMBER OF CIGARETTES SMOKED PER DAY BY PARENTS AND WINTER MORNING PHLEGM

Year of follow-up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis							
	Both non-smokers		One or both smokers* of following number of cigarettes per day:					
			1 - 14		15 - 24		25 and over	
	N	O/B	N	O/B	N	O/B	N	O/B
1	7.6 (343)	10.3 (39)	10.4 (269)	18.1 (83)	11.1 (171)	14.5 (76)	13.2 (322)	23.2 (138)
2	8.1 (322)	6.3 (36)	5.2 (221)	16.4 (55)	8.6 (151)	14.5 (62)	9.7 (269)	9.6 (164)
3	6.9 (305)	8.1 (37)	11.2 (269)	8.6 (70)	8.2 (146)	9.5 (42)	8.6 (243)	11.2 (161)
4	8.9 (287)	11.1 (36)	5.5 (163)	13.3 (45)	7.4 (136)	11.5 (52)	9.1 (243)	10.3 (126)
5	4.7 (285)	14.7 (34)	6.3 (144)	11.4 (44)	4.4 (159)	7.6 (53)	4.1 (218)	10.6 (142)

* Excluding parent pairs where one or both are ex-smokers or changed smoking habit.
** Includes stream and cigars expressed as cigarette equivalents (see Todd).
N = neither with winter morning phlegm. O/B = one or both with winter morning phlegm.

The authors also state:

"The infants of mothers who smoke in pregnancy are, on average, lighter than those of mothers who do not smoke. As infants of low birth-weight are more likely to suffer respiratory illness than normal-weight infants, it is possible that the gradients in respiratory disease observed in the first year of life, and in particular the effects of passive smoking, may be due, indirectly, to maternal smoking during pregnancy. In this study, birth-weight, as expected, shows a gradient by parents' initial smoking habit, and to a lesser extent by winter morning phlegm. Thus parents who smoke have lighter infants than parents who do not smoke. The gradients in the incidence of pneumonia and bronchitis with parental smoking, and with winter morning phlegm, might therefore be partly attributable to differences in birth-weight. However, within different birth-weight categories the gradients for pneumonia and bronchitis with parents' smoking habits persist. Thus differences in birth-weight cannot account for the higher risk of pneumonia and bronchitis in the first year of life in children exposed to the cigarette smoke generated when their parents smoke at home."

2021550815

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

In the discussion of their paper, the authors observe:

"Passive smoking by the infant, after differences in birth-weight and parental respiratory symptoms have been allowed for, increases the risk to the infant of pneumonia and bronchitis in the first year of life. When both parents smoke, this risk is almost double that of infants with non-smoking parents. The findings confirm and extend those of Harlap and Davies. These workers did not, however, have information on fathers' smoking habits, nor did they take account of parents' respiratory symptoms.

A picture has thus emerged of a serious risk to infants in the first year of life from exposure to their parents' cigarette smoke. In contrast, between one and five years of age, there does not appear to be any important effect of passive smoking in increasing the risk of pneumonia and bronchitis. Colley, in 6-14-year-olds also found no association between passive smoking and the prevalence of chronic cough.

The estimates of children's exposure to cigarette smoke in this study are crude, being based either on whether parents were smokers or not, or on their total daily cigarette consumption. The smoke exposure of the children may have been overestimated, since parents - in particular the father - will smoke outside the home, or at times when the infant is not present. The effects on the child may thus have resulted from exposure to levels of cigarette smoke less than those suggested by our study."

(c) Leeder et al. - Influence of family factors on the incidence of lower respiratory illness during the first year of life.

This article was published in 1976 in the British Journal of Preventive and Social Medicine. The authors were from the Department of Community Medicine at St Thomas's Hospital, Medical School, London and the Department of Community Health at Bristol. The following summary of the study appears in the article:

"In a study of a cohort of over 2000 children born between 1963 and 1965, the incidence of bronchitis and pneumonia during their first year of life was found to be associated with several family factors. The most important determinant of respiratory illness in these infants was an attack

2021550816

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

of bronchitis or pneumonia in a sibling. The age of these siblings, and their number, also contributed to this incidence. Parental respiratory symptoms, including persistent cough and phlegm, and asthma or wheezing, as well as parental smoking habits had lesser but nevertheless important effects. Parental smoking, however, stands out from all other factors as the one most amenable to change in seeking to prevent bronchitis and pneumonia in infants."

The authors reported some of their findings in the following terms:

"During the first year of life, the incidence of bronchitis and pneumonia varied according to several family factors. These illnesses occurred much more commonly in infants born to families which had several other children already, and in those families where the parents had respiratory disability or were smokers.

Children whose parents both had a history of asthma-wheeze had an incidence of bronchitis or pneumonia of 26.9% which was three times greater than that found in children of parents without such a history (9.4%) (Table III). The effect of parental smoking was not so great. The incidence of bronchitis or pneumonia in children of non-smoking parents was 7.2% compared with 17.7% when both parents smoked. When both smoking habits and asthma-wheeze were examined for combined effects on the incidence of bronchitis or pneumonia in the children, these contrasts widened. For example, the incidence of bronchitis or pneumonia was 6.7% in infants whose parents neither smoked nor had suffered from asthma-wheeze; this contrasted with an incidence of 39.3% when both parents smoked and had a history of asthma-wheeze."

..../150

2021550817

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

TABLE III

ANNUAL INCIDENCE PER 100 INFANTS OF BRONCHITIS OR PNEUMONIA IN THE FIRST YEAR OF LIFE BY PARENTAL HISTORY OF ASTHMA-WHEEZE AND SMOKING HABIT

		Parental Smoking Habit				
		Neither	One	Both	Habit Changed	Total
Parental asthma-wheeze	Neither	6.7 (451)	9.6 (502)	13.7 (314)	8.7 (241)	9.4 (1508)
	One	8.9 (101)	18.0 (178)	22.3 (139)	7.4 (81)	15.6 (499)
	Both	14.3 (7)	13.6 (22)	39.3 (28)	30.0 (10)	26.9 (67)
	Total	7.2 (559)	11.8 (702)	17.7 (481)	9.0 (332)	11.5 (2074)*

Populations in parentheses

* Total excludes 27 infants with missing first year data and an additional 48 with missing initial and first year data on parent pairs.

(d) Sims et al. - Study of 8-year-old children with a history of respiratory syncytial virus bronchiolitis in infancy.

This article appeared in the British Medical Journal in 1978. The authors were from the University of Newcastle upon Tyne. The contents of the article are of only marginal significance for present purposes. In the study, 35 children known to have had respiratory syncytial virus bronchiolitis in infancy were examined at the age of 8 and their respiratory function tested. The results were

2021550818

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

compared with those in 35 controls matched for age, sex, and social class. The authors concluded, inter alia, that the parents of the children who had had bronchiolitis smoked significantly more cigarettes during the infant's first year of life than those of the control children.

(e) Rantakallio - Relationship of maternal smoking to morbidity and mortality of the child up to the age of five.

The author of this article which was published in 1978 was from the Department of Paediatrics and the Department of Public Health, University of Oulu, Finland. The abstract of the article as published reads as follows:

> *"The effect of maternal smoking during pregnancy on the morbidity and mortality of the child up to the age of five was studied in 12 068 births. The children of the smokers were compared with those of controls of similar age, parity, marital status and place of residence. Perinatal mortality was no higher among the smokers, but postneonatal mortality from 28 days to 5 years was almost significantly ($p < 0.05$) higher. The children of the smokers were highly significantly ($p < 0.001$) more often hospitalized in pediatric departments, the difference being clearest below the age of one. The average duration of hospital admissions was longer among the children of the smokers, and similarly the numbers of visits to the doctor and hospital admissions to any hospital under the age of one were more frequent among the children of the smokers. Respiratory diseases caused highly significantly more hospitalizations among these children."*

Table 6 in the article refers to the incidence of diseases during the first 5 years among the children of the smokers and the controls in the study. With respect to this table the authors state:

> *"Table 6 presents the frequency of all disease groups diagnosed in children's departments per thousand live births among the children of smokers and of their controls. If the child had been in hospital more than once for the same disease it was counted only once. Respiratory and skin*

2021550819

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

diseases were more frequent among the smokers than among the controls, the difference being statistically highly significant .... Among the respiratory diseases the ratio of the incidence among the smokers to that of the controls was 2.2 in pneumonia, 1.8 in bronchitis, and 1.5 in others such as acute nasopharyngitis, sinusitis etc. ...

Under the age of one year the difference in the diseases was in general greater between the heavy smokers and their controls than between the light smokers and their controls, but this was no longer true for the age from one to five.

When the main causes of hospitalization in pediatric departments per thousand live births was calculated for both groups a statistically highly significant difference ($p < 0.001$) was found only in the case of respiratory diseases, and an almost significant difference ($p < 0.05$) in the case of skin diseases. The more frequent hospitalization of the children of smokers because of respiratory diseases was clearest below the age of one, but also existed at the age of one to five, the difference between the smokers and controls at that age being almost significant ($p < 0.05$). Again the children of the heavy smokers were more affected than those of the light smokers under the age of one, but not at the age of one to five."

(f) Fergusson et al. - Parental smoking and respiratory illness in infancy

The authors of this article which was published in 1980 were from the Department of Paediatrics, Christchurch Hospital, New Zealand.

The data for the study were collected during the third stage of a study known as the Christchurch Child Development Study. In the project a cohort of infants was studied at birth, at four months and at one year.

The summary of their article reads as follows:

"The relationship between parental smoking and respiratory illness in a birth cohort of 1180 one-year-old children was examined. Maternal smoking was associated with an increased incidence of lower respiratory illness but there was no statistically significant association between paternal

2021550820

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

smoking and lower respiratory illness. While children of mothers who smoked suffered more lower respiratory illnesses, their overall risk of respiratory infection was similar to that for children of nonsmoking mothers. The association between maternal smoking and infantile lower respiratory illness persisted when the child's social background, perinatal history, and postnatal diet were taken into account. The findings favour the view that prolonged exposure to cigarette smoke predisposes infants to develop lower respiratory symptoms when they contract a respiratory infection."

In their discussion of their paper, the authors make the following statements:

"Previous studies have considered the effects of parental smoking on lower respiratory illness only. The findings reported here show that there is a complicated relationship between parental smoking and all respiratory illness. Overall, the children of mothers who smoke do not have a greater risk of respiratory illness but they do have a greater risk of suffering respiratory illness affecting the lower respiratory tract. This finding suggests that the effect of maternal smoking is to irritate the infantile lung and thus facilitate the spread of infection to the lower respiratory tract.

In addition, previous research has examined the relationship between parental smoking and medical consultation for lower respiratory illness. Since medical consultations probably provide a biased sample of infant illness, there is the possibility that the apparent association between parental smoking and infant lower respiratory illness could have arisen from some bias in consulting practices. The results reported here show that this is unlikely to be the case: an association between maternal smoking and infantile lower respiratory illness has been shown to exist both for illness needing medical treatment and for maternal reports of lower respiratory symptoms, irrespective of whether these symptoms were treated by a medical practitioner.

Finally, the range of social and perinatal factors controlled in this study is greater than that considered in previous studies of the topic. On the basis of the findings reported here, it may be concluded that the association between maternal smoking and infantile lower respiratory illness cannot be explained by the confounding effects of such factors as adverse perinatal history, depressed social background, or bottle feeding.

There now appears to be sufficient evidence to support the view that people in regular and prolonged contact with infants should not smoke, or if they must, they should not do so in the presence of infants."

2021550821

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

(g) **Fergusson et al** - Parental smoking and lower respiratory illness in the first three years of life.

The authors of this study (save for one additional co-author) were also the authors of the previous study. The article was published in 1981. The following summary of the study appears in the article:

> *"The relationships between parental smoking and the rates of lower respiratory illness during the first three years of life were examined for a birth cohort of 1265 New Zealand children. Lower respiratory illness varied significantly with maternal smoking for the first year; there was equivocal evidence of a relationship between maternal smoking and lower respiratory illness in the second year; and by the third year the relationship had clearly disappeared. Paternal smoking had no significant effect on rates of lower respiratory illness at any time.*
>
> *Application of logistic regression showed that for the first year rates of lower respiratory illness were approximately linearly related to maternal smoking: increases of five cigarettes a day resulted in an increase of 2.5 to 3.5 incidents of lower respiratory illness per 100 children at risk. Statistical control for maternal age, education, family size, and family living standards showed that the relationship between maternal smoking and rates of lower respiratory illness was not significantly influenced by these factors."*

..../155

2021550822

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Table 2 of the report is as follows:

Table 2 Rates per 1000 children of bronchitis/pneumonia and lower respiratory symptoms in the first three years of life by maternal and paternal smoking (number of children in brackets)

Paternal smoking (cigs/day)	BRONCHITIS/PNEUMONIA			LOWER RESPIRATORY SYMPTOMS		
	Maternal smoking (cigs/day)			Maternal smoking (cigs/day)		
	0	1-10	11 +	0	1-10	11 +
FIRST YEAR	FIRST YEAR	FIRST YEAR	FIRST YEAR	FIRST YEAR	FIRST YEAR	FIRST YEAR
0	7.0 (568)	12.8 (78)	13.4 (112)	37.8 (566)	47.4 (76)	39.8 (113)
1-10	4.8 (83)	14.0 (43)	11.1 (18)	37.9 (83)	53.5 (43)	55.6 (18)
11 +	8.8 (136)	12.7 (59)	19.7 (61)	48.4 (169)	43.8 (59)	55.1 (61)
SECOND YEAR	SECOND YEAR	SECOND YEAR	SECOND YEAR	SECOND YEAR	SECOND YEAR	SECOND YEAR
0	6.1 (644)	20.7 (97)	13.2 (114)	49.6 (566)	64.0 (97)	50.9 (113)
1-10	7.9 (76)	3.8 (26)	12.0 (83)	44.7 (76)	51.9 (81)	39.0 (26)
11 +	11.1 (109)	15.9 (44)	11.9 (67)	53.6 (109)	56.2 (46)	50.8 (67)
THIRD YEAR	THIRD YEAR	THIRD YEAR	THIRD YEAR	THIRD YEAR	THIRD YEAR	THIRD YEAR
0	8.8 (606)	5.6 (72)	12.1 (116)	37.4 (606)	38.7 (73)	46.3 (117)
1-10	11.8 (76)	6.7 (29)	6.0 (29)	41.8 (77)	21.7 (23)	38.0 (29)
11 +	12.2 (106)	13.5 (67)	9.1 (66)	38.1 (106)	40.5 (37)	41.8 (66)

In their discussion of their work the authors observe:

"*In confirmation of the findings of Colley et al the correlation between parental smoking and childhood lower respiratory illness appeared to be most marked for the first year of life and showed a steady decline with increasing age. At one year, clear differences between the offspring of smokers and non-smokers were evident; at two years the evidence was equivocal; and by three years an association between maternal smoking and infant lower respiratory illness was clearly absent. However, these findings are not entirely consistent with reports which have shown greater rates of respiratory problems (morning cough and breathlessness) among children of school age with smoking parents. One hypothesis which satisfies the available data is that the effect of parental smoking on childhood lower respiratory illness and symptoms is two-fold. During early life, and particularly the first year, prolonged contact with cigarette smoke would*

2021550823

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

appear to precipitate or exacerbate lower respiratory illness in children; this effect is relatively short-lived and disappears at the age of about 2. However, prolonged exposure to cigarette smoke over a period of years may have a compound interest effect in compromising the respiratory function of children, with the result that by the time middle childhood is reached, children of smokers have a greater rate of lower respiratory illness or symptoms."

(h) Ekwo et al - Relationship of parental smoking and gas cooking to respiratory disease in children.

The authors of this article, which was published in 1983, are from the University of Iowa Medical School.

The authors found that the risk of hospitalisation for respiratory illness in children before age 2 years was increased when at least one of the parents smoked. The authors concluded that, based on the findings of their report and from previously published findings, "one is led to conclude that parental smoking is associated with a risk of certain respiratory illnesses and symptoms among children living in the same environment."

(j) Schenker et al - Risk factors for childhood respiratory disease. The effect of host factors and home environmental exposures.

The authors of this article which was published in 1983 were from the Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston and the Department of Medicine, University of New Mexico School of Medicine.

2021550824

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Many of the findings of this study relate to matters of no present concern. However, the authors concluded that chest illness before two years of age showed a significant positive linear trend with the number of parental smokers.

(k) Ware et al. - Passive smoking, gas cooking, and respiratory health of children living in six cities.

The authors of this study which was published in 1984 were from the Harvard School of Public Health, the Harvard Medical School and Brigham and Women's Hospital, Boston. Part of the summary which appears in the article is as follows:

> *"As part of a longitudinal study of the respiratory health effects of indoor and outdoor air pollutants, pulmonary function, respiratory illness history, and symptom history were recorded at 2 successive annual examinations of 10,106 white children living in 6 cities in the United States. Parental education, illness history, and smoking habits also were recorded, along with the fuel used for cooking in the child's home. Maternal cigarette smoking was associated with increases of 20 to 35% in the rates of 8 respiratory illnesses and symptoms investigated, and paternal smoking was associated with smaller but still substantial increases. Illness and symptom rates were linearly related to the number of cigarettes smoked by the child's mother. Illness rates were higher for children of current smokers than for children of ex-smokers. The associations between maternal smoking status and childhood respiratory illnesses and symptoms were reduced but not eliminated by adjustment for parental illness history. Levels of forced expiratory volume in one second (FEV_1) were significantly lower for children of current smokers than for children of nonsmokers at both examinations and highest for children of ex-smokers. Levels of forced vital capacity (FVC) were lower for children of nonsmokers than for children of current smokers at both examinations, but the difference was statistically significant only at the first examination. Both the increase in mean FVC and the decrease in mean FEV_1 among children of current smokers were linearly related to daily cigarette consumption. ... These results provide strong support for a causal effect of sidestream cigarette smoke on increased respiratory illness and reduced FEV_1 values in preadolescent children."*

202155082S

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

The authors explain the methodology of their study in considerable detail and make the following observations on their analyses of the data collected:

> *"These analyses show a consistent association between parental cigarette smoking and increased respiratory illness during childhood. Of the children in this sample, 43% had mothers who were current smokers (table 4), 59% had fathers who were current smokers, and 68% had at least one parent who was a current smoker. Thus, effects of sidestream cigarette smoke of the size observed in this study would represent a substantial public health burden.*
>
> *Current maternal cigarette smoking was associated with a 20 to 35% increase in the risk of all respiratory illnesses and symptoms in the past year. A history of either parent smoking was associated with a similar increase in the reported prevalence of early childhood respiratory illness. Each of these respiratory health indexes is linearly related to the current amount of cigarette smoking by either both parents or the mother alone. In all of these analyses, the association between impaired health and passive smoke exposure was stronger with maternal than with paternal or total parental smoking. Children of ex-smokers had respiratory illness and symptom frequencies that were typically between those of nonsmoking and currently smoking mothers. This was true for recent illness and symptom experience, as well as for early childhood illnesses. These findings are consistent, at least in part, with the hypothesis that exposure to cigarette smoke increases the risk of contemporaneous respiratory illness."*

After referring to the stronger association with maternal rather than paternal smoking for respiratory illness in childhood, the authors state:

> *"The somewhat stronger association of respiratory illness with maternal than with paternal smoking habits need not imply any special risk associated with maternal smoking. A more plausible interpretation is that the risk factor is exposure to sidestream cigarette smoke, and that children are more likely to be with their mothers than with their fathers at the times smoking occurs."*

2021550826

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

(l) Pedreira et al. - Involuntary smoking and incidence of respiratory illness during the first year of life

The authors of this article were from the Department of Paediatrics at the George Washington University School of Medicine, Washington, DC. The article was published in 1985. The following summary of the study appears in the article:

> *"A prospective study of 1,144 infants and their families was performed. Smoking and family histories were evaluated with respect to the incidence of lower respiratory disease during the first year of life. It was found that (1) tracheitis and bronchitis occurred significantly more frequently in infants exposed to cigarette smoke in the home, (2) maternal smoking imposed greater risks upon the infant than paternal smoking, (3) occurrence of neither tracheitis nor bronchitis showed a consistent relationship to the number of cigarettes smoked, (4) a family history that was positive for respiratory illness (chronic cough or bronchitis) significantly influenced the incidence of bronchitis, (5) too few cases of laryngitis and pneumonia were seen to warrant any opinions regarding the adverse influence of either smoking or a family history that was positive for respiratory illness, and (6) occurrence of bronchiolitis was not affected by the presence of a smoker nor influenced by a family history that was positive for respiratory illness. It is concluded that passive smoking is dangerous to the health of infants and that infants born to families with a history that is positive for respiratory illness (chronic cough or bronchitis) are at risk of developing bronchitis."*

(m) Chen et al. - Influence of passive smoking on admissions for respiratory illness in early childhood

The authors of this article were from the Department of Epidemiology, School of Public Health, Shanghai Medical University, Shanghai. The article was first published on 2 August 1986 in the British Medical Journal but was accepted for publication in April 1986.

The following summary of the study appears in the article:

2021550827

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

"An association was sought between passive smoking and in-patient admissions for respiratory illness in 1058 children born between 1 June and 31 December 1981 and living in the neighbourhoods of Nan-Jing Western Road and Yan-An Western Road in Jing-An District, Shanghai. The admission rate for first episodes of respiratory illness was positively correlated with the total daily cigarette consumption of family members during the children's first 18 months of life. The relative risk of developing a first episode of respiratory illness was 1.80 for children living in families including people who smoked 10 or more cigarettes a day compared with those living in non-smoking families. Multiple logistic regression analysis showed that the effect of passive smoking on inpatient admission for respiratory illness was independent of the child's birth weight, type of feeding, father's education, size of the home, and chronic respiratory disease among adults in the family. The adjusted odds ratios compared with the non-smoking group were 1.17 in families smoking 1-9 cigarettes daily and 1.89 in families smoking 10 or more cigarettes daily.

These data suggest that exposure to household cigarette smoke of children in early life increases the risk of severe respiratory illness."

(n) Taylor and Wadsworth - Maternal smoking during pregnancy and lower respiratory tract illness in early life

The authors of this article, which was received for publication on 27 February 1987, were from the Department of Child Health at the University of Bristol and the Departments of Paediatrics and Community Medicine at St Mary's Hospital Medical School, London.

The following summary of the study appears in the article:

"In a national study of 12 743 children maternal, but not paternal, smoking was confirmed as having a significant influence on the reported incidence of bronchitis and admission to hospital for lower respiratory tract illness during the first five years of life. Reported rates of admissions to hospital for lower respiratory tract diseases were found to be as high in children born to mothers who stopped smoking during pregnancy as in those whose mothers smoked continuously both during and after pregnancy. Rates of admissions to hospital for lower respiratory tract diseases in children whose mothers started smoking only postnatally were no higher

2021550828

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

than in those whose mothers remained non-smokers. Postnatal smoking seemed to exert a significant influence on the reported incidence of bronchitis, but less than smoking during pregnancy.

These findings suggest that maternal smoking influences the incidence of respiratory illnesses in children mainly through a congenital effect, and only to a lesser extent through passive exposure after birth."

(ii) The major reviews

(a) The Surgeon General's Report

The Surgeon General examined a number of studies, based on a variety of different designs, examining the effects of involuntary smoking on the acute respiratory illness experience of children. Most of the studies contained in the primary articles are considered by the Surgeon General. He summarises his assessment of these studies as follows (p.44):

"In summary, the results of these studies show excess acute respiratory illness in the children of parents who smoke, particularly in children under 2 years of age. This pattern is evident in studies conducted with different methodologies and in different locales. The increased risk of hospitalization for severe bronchitis or pneumonia associated with parental smoking ranges from 20 to 40 percent during the first year of life. Young children appear to represent a more susceptible population for the adverse effects of involuntary smoking than older children or adults. The time-activity patterns of infants, which generally place them in proximity to their mothers, may lead to particularly high exposures to environmental tobacco smoke if the mother smokes."

The Surgeon General's Report contains a table (Table I) in which the studies are summarised. Although the table contains some references which are elliptical, I set it out so as to show the material upon which the Surgeon General based his conclusions.

2021550829

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

2021550830

TABLE 1. - Early childhood respiratory illnesses and involuntary cigarette smoking

Study	Subjects	Findings	Illness rate per 100				Comments
			By cigarettes per day				
			0	1-10	11-20	20 +	
Hadap and Davies (1974)	10,672 births, 1965-1966 Israel	Hospitalized, bronchitis/ pneumonia, first year of life RR = 1.38	8.5	10.8	16.2	31.7	Parental smoking history; maternal smoking only Longitudinal study
Colley [1]	2,205 births, 1963-1965 England	Questionnaire, bronchitis/ pneumonia, first year of life RR = 1.75 for one parent smoker RR = 2.04 for two parent smokers	7.6 18.3	10.4 15.1	11.1 14.5	15.2 23.2	= Asymptomatic parents = Symptomatic parents Neither controlled for sibling or mother not Longitudinal study
Ferguson et al. (1981); Ferguson and Horwood (1985) [2]	1,265 births, 4 months 1977, New Zealand	Questionnaire, doctor or hospital visits, bronchitis/pneumonia; hospital records checked; assessed at 4 months, 1, 2, 3, and 6 years; RR = 2.04 if mother smoked	7.0 7.0	12.8 4.6	13.4 8.8	Maternal only Paternal only	Effect significant for maternal smoking in first year of life only; effect present in first 2 years of life
			By number of smoking parents				
			0	1	2		
Ware et al. (1984)	8,528 children, aged 5-9, with two parents' smoking status known, six U.S. cities	Respiratory illness in last year	12.9	13.7	14.8		Adjusted for age, sex, and city cohort effect; significant trends Longitudinal study
Said et al. (1978)	3,920 children, aged 10-20, France	Tonsillectomy and/or adenoidectomy, generally before age 5, as indicator of frequent respiratory tract infection	28.2	41.4	58.9		Children self-reported; not clear parent smoking habit at report time directly related to exposure approx. 10 + years earlier Cross-sectional study
Schenker et al. (1969)	4,871 children, aged 5-14, United States	Chest illness before age 2 Chest illness > 3 days in past year	6.7 8.8	7.9 11.8	11.5 13.6		Trends for both significant Cross-sectional study

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Study	Subjects	Findings		Illness rate per 100		Comments
				Parent status		
				Nonsmoker	Current smoker	
Cameron et al.	158 children, aged 4-9; parent' telephone questionnaire, United States	Respiratory illness, restricted activity and/or medical consultation in last year		1.33	2.4	Illness reported not verified; not clear how reporting adult related to child Cross-sectional study
Lander et al. (1976a, b)	2,149 infants, born 1963-1965, England	RR = 2.0 for infants with two smoking parents		Not provided		Parents' response bias unlikely, effects observed for infants of asymptomatic parents; maternal vs. paternal smoking effects not investigated Longitudinal study
Shaw et al. (1978)	35 children, hospitalized, RSV bronchiolitis; 35 controls, England	Borderline significant increase in maternal smoking, first year of life: RR = 2.65		Not provided		No significant effect for paternal smoking; average amount smoked greater for parents of cases than controls Case-control study
Ramotallio (1978)	1,821 children of smoking mothers, 1,823 children of nonsmoking mothers, Poland	Significant increase in hospitalization for respiratory illness during first 5 years of life: RR = 1.74		Not provided		Prospective followup of doctor visits, hospitalizations, deaths up to age 5; only maternal smoking evaluated Longitudinal study
Pullan and Hey (1982)	150 children hospitalized, RSV infection, first year of life; 111 nonhospitalized controls, England	Significant effect of maternal (RR = 1.96) and paternal (RR = 1.53) smoking at time of study; significant maternal smoking effect during first year of life (RR = 1.55)		Not provided		Case -control study
Pedreira et al. (1985)	1,186 infants in pediatric practice, United States	Significant increase in respiratory illnesses among smoke-exposed children		Nonsmoker	Smoker	Pediatricians not blinded to exposure; no effect seen for croup, pneumonia, or bronchiolitis Longitudinal study
			Bronchitis	71	910	
			Tracheitis	21	48	
			Laryngitis	4	7	

[1] These data are considered in a more expanded analysis provided by Lander et al. (1976 a, b).

[2] Relative risk for children of smoking mothers versus children of nonsmoking mothers calculated from data provided by J.M.Sinnet (personal communications).

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

The Surgeon General also examined studies as to the association between parental cigarette smoking and prevalence of chronic cough, chronic phlegm and persistent wheeze in children. His conclusion was as follows (p.48):

> *"In summary, children whose parents smoke had a 30 to 80 percent excess prevalence of chronic cough or phlegm compared with children of nonsmoking parents. For wheezing, the increase in risk varied from none to over sixfold among the studies reviewed. Many studies showed an exposure-related increase in the percentage of children with reported chronic symptoms as the number of parental smokers in the home increased. Misclassification as nonsmokers of children who are actively smoking could bias the results of these studies. Adolescent smokers may be reluctant to accurately report their smoking habits, and more objective measures of exposure may not help to distinguish active experimentation with cigarettes from involuntary exposure to smoke (Tager 1986). Although misclassification of children who are actively smoking as nonsmokers must be considered, many studies showing a positive association between parental smoking and symptoms in children, including children at ages before significant experimentation with cigarettes is prevalent. In addition, many studies (Bland et al. 1978; Weiss et al. 1980; Charlton 1984; Schenker et al. 1983; Dodge 1982; Burchfiel et al. 1986) found significant effects of parental smoking after considering active smoking by the children."*

(b) <u>The National Research Council report</u>

At p.9 of this report the following appears:

> *"Respiratory symptoms, such as wheezing, coughing, and sputum production, are increased in children of smoking parents. These symptoms are more common in children of smokers than children of nonsmokers. The largest studies place the increased risk of 20 to 80%, depending on the symptom being assessed and number of smokers in the household. Also, respiratory infections manifested as pneumonia and bronchitis are significantly increased in infants of smoking parents. Some studies have reported that infants of smoking parents are hospitalized for respiratory infections more frequently than children of nonsmokers. Among children aged under 1 year, studies are remarkably consistent in showing an increased risk of respiratory infections among children living in homes where parents smoke. There is a dose-response relationship that relates more to maternal smoking than paternal smoking. The association persists after allowing for possible confounding factors such as occupational data,*

2021550832

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

respiratory illness in the parents, and birthweight. The mechanisms of the increased risk may either be a direct effect of ETS or due to a higher risk of cross-infection in such homes. Regardless of the mechanism, the exposure of small children to smoking in the home appears to put them at risk of respiratory illness."

In the body of the report particular attention is given to the possibility of under-reporting of active smoking on the part of children, recall bias leading to over-reporting of symptoms by parents, and the confounding variables of infections in parents. All three of these may lead to an over-estimation of symptom prevalences among children of smokers. However, after considering studies that have compared children of parents who smoke with children of parents who do not smoke and after referring to a finding that adjustment for parental symptoms or respiratory illness decreases the strength of the apparent association between exposure to environmental tobacco smoke and respiratory symptoms, but does not eliminate it, the authors state:

"This finding leads to the reasonable conclusion that the exposures typical of ETS are sufficient to cause respiratory symptoms in some children. The increases in frequency of cough were 20 to 50%, and as high as 90%, when there were smoking parents. The increases in frequency of wheezing were more variable, which may indicate the difficulty in assessing this symptom. Furthermore, there appears to be a dose-response relationship between exposure and the likelihood of the child's developing respiratory symptoms or a respiratory illness."

(c) <u>The National Health and Medical Research Council report</u>

The following are extracts from chapter 5 of this report, which deals with Passive Smoking and Child Health. I have omitted references to some of the footnotes in the text of the report:

2021550833

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

"Several adverse health effects resulting from passive smoking during childhood have been demonstrated. Children who receive a heavy passive exposure to cigarette smoke have more symptoms and disability from respiratory tract infection than other children. Although many controlled studies have shown this increased prevalence of respiratory symptoms in children of smoking mothers, this observation is not universal.

The best longitudinal cohort studies, adjusted for confounding variables, document that there is approximately twice the incidence of respiratory symptoms and disability due to respiratory disease in smokers' children in the first year of life, compared to children of non-smokers. In fact, no study negates this observation in the first year of life. However, the relationship is less certain at later ages."

The summary of the chapter in the report on Passive Smoking and Child Health is expressed in the following terms:

"Smoking during pregnancy has a clear detrimental effect on the fetus. A consistent association of passive smoking with respiratory morbidity in children has been reported in a number of studies, based on different populations, using different study designs with a variety of outcome measures. There is strong evidence to suggest that maternal smoking is associated with increased lower respiratory symptoms in the first year of life. Associations of passive smoking with respiratory symptoms, reduced lung function, or asthma symptoms in later childhood have been suggested, but the changes are small. Additional longitudinal studies will be required to determine whether these changes are clinically significant.

Smoking and non-smoking families differ in various respects and, although such differences have been recorded and adjusted for in many studies, it remains possible that some of the apparent effect of passive smoking arises from other environmental or behavioural confounding factors that have not been adequately controlled. Further, it is not known whether young children respond more to these irritants, nor whether observed effects of passive smoking reflect predominantly a small effect in large numbers or a larger effect in a susceptible subgroup.

Passive smoking does appear to have some detrimental effect on health at most ages from conception to adolescence. A dose-response relationship with increasing maternal smoking rate found in a number of studies makes a causal link between passive smoking in infancy and respiratory illness, abnormal lung function in childhood, increased asthmatic symptoms and impaired growth seem likely. Further longitudinal studies should help clarify these observations."

2021550834

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

(iii) Oral evidence

(a) Professor Landau

Professor Louis Landau is a respiratory physician. He has been Professor of Child Health in the University of Western Australia since 1984. He was at one time Principal Research Fellow at the Royal Children's Research Foundation, Melbourne and is a former Head of the Professorial Department of Thoracic Medicine at the Royal Children's Hospital, Melbourne. The professor's clinical work is concerned exclusively with children with respiratory disorders. He has had considerable experience in clinical work.

In the course of his clinical experience over the past 15 years Professor Landau has examined and treated numerous non-smoking patients whose conditions and diseases were, in his view, directly or indirectly attributable to exposure to passive smoking. He is of the opinion that there is evidence which proves scientifically that cigarette smoke causes disease in non-smokers.

Professor Landau is of the opinion that tobacco smoke can harm children because of the effect of, inter alia, passively inhaled smoke. He said that measurements of continine in the secretions of children exposed to environmental tobacco smoke indicate significant intake of compounds which could exert a detrimental effect on their health. He said that although there is some variability in the measurements, there is a consistency of some effect and a dose-response to environmental tobacco smoke.

2021550835

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

According to the professor, children who receive a heavy exposure to cigarette smoke have more symptoms and disabilities from respiratory illness than others. He believes that the best studies, adjusted for confounding variables, document at least double the incidence of respiratory symptoms in the first year of life. In his opinion, cigarette smoke may also have an adverse effect on the health of children with pre-existing lung disease. He said that a dose-response relationship and the presence of high levels of cotinine in secretions from the children exposed to passive smoking make a causal link between passive smoking and, inter alia, respiratory disease seem very likely.

Professor Landau was the principal author of Chapter 5 of the NH and MRC report. He said that his views, as I have summarised them above, were held by him as at July 1986.

He gained particular support for his opinions from the primary articles by Harlap and Davies, and by Fergusson et al. However, he referred to many other primary articles in his evidence, and drew support from them.

As will be seen when I refer to the evidence of Dr Witorsch as to the relationship between passive smoking and respiratory disease in children, there does not appear to be much difference between his and Professor Landau's views as to the effect of passive smoking on children in the first year of life.

2021550836

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Professor Landau was cross examined as to his views, but, in my opinion, they were not shown to be in any way erroneous. He was asked very little about the effect of passive smoking on children under the age of one year. He was cross examined at some length as to the reasons why the first draft of part of the NH and MRC report had been altered. This part did not relate to respiratory symptoms in children in the first year of life. In any event, the professor's explanation of the making of the alteration leaves me in no doubt that it was properly made.

Professor Landau was cross examined at some length about the Harlap and Davies study. He agreed (T.2136) that it pointed to the need for more and more detailed studies on the subject. However, he said the study gave information which needed to be confirmed and which was subsequently confirmed, by other studies.

Professor Landau limited his assertion that there was scientific proof that passive smoking causes disease to the causation of respiratory disease in children under the age of 12 months. But he said (T.2060):

> *"I think once we get beyond the first year of life the associations are strong, consistent, but it would be harder to use the definition of scientific proof in them ..."*

(b) Dr Le Soeuf

Dr Peter Le Soeuf is Director of the Department of Respiratory Medicine at Princess Margaret Hospital for Children, Perth. He has had extensive experience in paediatrics. He was formerly a Research Fellow in the Respiratory Physiology Department of the Hospital for Sick Children, Toronto, Canada. He has

2021550837

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

been a Fellow in Paediatric Respiratory Medicine at the Royal Children's Hospital, Melbourne. He has held his present position for the last six years during which time he has been a Senior Lecturer in the Department of Paediatrics at the University of Western Australia. He is the co-author of a large number of learned articles mostly related to respiratory functions in children.

Dr Le Soeuf is of the opinion that there is very strong scientific evidence that the passive inhalation of cigarette smoke causes disease in young children. He bases his opinion on his professional and clinical experience as a paediatrician and upon his reading of the scientific literature. He said that in the course of his clinical experience and in his capacity as a consultant respiratory physician, he has examined and treated 40 young children whose condition or disease was in his view directly or indirectly attributable to exposure to passive smoking. He said there is an abundance of pathological, clinical and epidemiological evidence suggesting that passive smoking is an important and significant cause of respiratory illness in infants and young children.

In Dr Le Soeuf's opinion, the strongest evidence of a causal relationship between passive smoking and respiratory disease is found in studies of infants in the first year of life. He thinks that the studies of children in this age group had detected a relationship between parental smoking and respiratory problems. He said that a significant relationship between passive smoking and respiratory disease or impaired lung function in children beyond the age of infancy had also been found, but such

2021550838

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

relationship has not been found in every study involving older children. He summarised his view as follows:

> *"In summary, there is a great deal of data from many different sources implicating passive smoking as a cause of respiratory disease in children. The strongest data is in the first year of life; every study in this age group has found that respiratory problems and passive smoking are significantly related. Overall, the data are so strong that in my opinion the possibility that passive smoking is not related to respiratory illness in young children is now excessively remote."*

. (Annexure "E" to his affidavit)

Dr Le Soeuf said that as a consultant paediatric respiratory physician he has seen many children, mostly asthmatic children over five or six years of age, who report that cigarette smoke exacerbates their respiratory symptoms, and that accordingly they move away from smokers. He said that more than half the children he sees are unable to recognise the effect on them of smoke and are likely to remain in the vicinity of smokers. It is his opinion that there are several infants under his care who have required hospitalisation due to their parents' cigarette smoke.

Dr Le Soeuf has great experience in the treatment of children. He estimated that he sees about 500 each year. He agreed that his statement that he had treated 40 young children whose condition was directly or indirectly attributable to exposure to passive smoking was an assessment based on his general experience, rather than on case histories of particular patients.

Dr Le Soeuf was cross examined at length as to the reliability of some of the studies upon which he placed reliance, particularly that of Harlap and Davies. But I do not think that it was shown that the studies were unreliable. Nor do I think

2021550839

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

that the cross examination of him showed that his opinion as to the effect of passive smoking on very young children was unsound.

(c) Dr Nolan

Dr Terence Nolan is Senior Lecturer in the Department of Paediatrics at the University of Melbourne. Amongst his other qualifications, he holds the Degree of Doctor of Philosophy from the Department of Epidemiology and Biostatistics at McGill University. Dr Nolan lectures in Theoretical and Applied Epidemiology to students who are pursuing the Degree of Master of Science in Epidemiology.

According to Dr Nolan, the epidemiological evidence of adverse health effects due to passive cigarette smoking on infants and children is considerable. In his opinion, in most cases the available evidence, apart from being abundant, is consistent, plausible and "temporally appropriate", i.e. one can be sure that exposure has preceded the onset of disease.

In his opinion, passive exposure to cigarette smoke increases the risk of respiratory illnesses, such as pneumonia, bronchiolitis, bronchitis, tracheitis and laryngitis in infancy and early childhood, at least during the first two years of life.

Dr Nolan is of the opinion that the findings referred to in the primary articles cannot reasonably be explained by bias in investigational methods, nor attributed to chance, nor reasonably explained by other factors.

2021550840

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Dr Nolan said that the opinions which he now holds were also held by him as at July 1986.

Dr Nolan made particular reference to the studies by Colley, Fergusson et al., Harlap and Davies, Pedreira and Rantakallio. Cross examination did not, in my opinion, reveal any important deficiencies in these studies or show that Dr Nolan was not justified in placing reliance upon them. I formed the opinion that Dr Nolan was particularly skilled in his specialist field.

(d) Professor Phelan

Professor Peter Phelan has been Professor and Chairman, Department of Paediatrics, Melbourne University since 1983. He has been Chief Thoracic Physician at the Royal Children's Hospital, Melbourne since 1983. He has had a great deal of experience extending over many years in the treatment of children. For some years he was a Research Fellow in the Clinical Research Unit at the Royal Children's Hospital Research Foundation. He has been a visiting Professor in the Institute of Child Health at the University of London and an Honorary Consultant Physician at the Hospital for Sick Children, Great Ormond Street, London.

Professor Phelan said that there are many studies that indicate that the incidence of lower respiratory tract infection in children, particularly in the first one or two years of life, is increased amongst those exposed to cigarette smoke. Maternal smoking seems to have a much stronger effect than paternal smoking.

2021550841

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

He said that evidence of an association between parental cigarette smoking, particularly domestic exposure, and respiratory illness in children is overwhelming. When challenged on this statement, he said that:

> *".... I think it is the volume - the consistency of the studies that I have referred to, and in many of them the very large numbers that together, in the view of experienced epidemiologists, say the evidence is overwhelming."*
>
> (T.1668)

He also said that it was his view that there is "extremely strong overwhelming evidence that there is an association between parental smoking and various types of respiratory illness in children" (T.1669).

He was cross examined about this statement and his evidence included the following (T.1670-71):

> *"Now, by 'overwhelming' do you mean to suggest to his Honour that competent, well-informed, and reputable epidemiologists, expert in this area, namely, childhood respiratory disease and exposure to cigarette smoke could not consistently with those quality (sic) hold the view that it was less than overwhelming?---I cannot speak for every reputable epidemiologist with interest in this area. All I could say, I would find it very difficult to perceive how someone who has studied the subject could come to a different conclusion. But I cannot say that someone may not."*
>
> (The word "quality" in the above question is, I think, wrongly attributed in the transcript to the cross examiner. The reference should be to "studies").
>
> *"Are you intending to suggest to his Honour perhaps that it is beyond debate so far as you are concerned?---Certainly, as far as I am concerned, it is beyond debate.*
>
> *For how long has it been beyond debate so far as you are concerned?---I think the studies became available from the mid-70s onwards, and certainly*

2021550842

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

by the early '80s, and definitely by the mid-80s I believed it was a subject beyond debate, as far as I personally am concerned.

What are the mid '80s? 1983 to 1988? 1987?---1984, 1985.

So, by 1984 or thereabouts, you tell his Honour, you regarded the question of an association between childhood respiratory illness and exposure to cigarette smoke as being beyond debate. Is that correct?---I believed at that stage that the evidence was very convincing.

And when I refer to 'debate' I am, of course, referring to debate amongst honest, competent, relevantly expert scientists. Do you understand that?---I understand what you are saying and - - -

Is that what you are saying, that by 1984, in your opinion, this question was beyond such debate?---I believed, with my recall of what evidence was available - and I would have to go back and check precise dates - but by the mid 1980s as I used (sic), that evidence was extremely convincing. Now, I cannot say that there would not be people who wish to take the opposite view. There are always in this world people who may wish to take an opposite view. But it certainly was a consensus of the people with whom I came in contact in the field of paediatric respiratory disease believed that evidence was convincing.

Now, you have referred to people who will always take an opposite view. Do you mean by that to suggest to his Honour that people who disagree with your view are ornery persons who would disagree for the sake of disagreeing ---?Not necessarily.

Do you agree that there - it is true to say that, as at 1 July 1986, it was open to reputable, competent, well-informed epidemiologists and medical scientists, expert in the area of respiratory disease in children and exposure to cigarette smoke, to believe that there was, in fact, little evidence of an association?---I would not agree with that statement."

In his opinion, it would be extremely difficult for someone who stood back and objectively looked at the evidence to come to any conclusion but that there is an association between exposure to cigarette smoke in a domestic environment and respiratory illness in children (T.1669).

Professor Phelan referred, as did the other witnesses in the applicant's case, to the many epidemiological studies tendered in evidence. I do not think any

2021550843

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

useful purpose would be served by further reference to them in these reasons. He noted some criticisms which could be made of some of the studies and took account of them. I much prefer his assessment of them to those made by the respondent's witnesses. He described the Fergusson et al. study as "a very well undertaken epidemiological study" (T.1009-10). He was extensively cross examined as to this study but I do not think his evaluation of it was shown to be wrong.

Professor Phelan was asked to explain how the views expressed in evidence could be reconciled with views he had expressed in a recent edition of a textbook of which he was co-author. In the book the following passage appears:

> *"Uncertainty remains as to the reasons for the relationship between parental smoking, parental winter phlegm and childhood respiratory illness. It is possible that the relationship is due to a similar genetic background. The presence of parental phlegm could increase the risk of cross-infection. Passive inhalation of tobacco smoke itself may be a cause of respiratory damage. Whatever the mechanism, parental cigarette smoking is a major risk factor for lower respiratory infection in infants and children."*

Professor Phelan said that he and his co-authors were too careful in writing that passage and that if he was writing it again he would have written it differently. The book was first published in 1975 and the second edition appeared in 1982. Professor Phelan said that, in retrospect, he thought that the section of the book from which the above quotation is taken should have been re-written.

I do not think the weight of Professor Phelan's evidence was lessened by the reference to the quotation from the book first written in 1975. For the purpose of this case, I am most concerned with his views as to the effect of respiratory illness in

2021550844

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

children in the first year or so of life. I do not think the statement in the third edition of his book, which refers to childhood respiratory illness in general, diminishes the weight of his evidence on the matter with which I am mostly concerned.

(e) Professor Witorsch

I have referred elsewhere to Professor Witorsch's qualifications and experience. The bulk of Professor Witorsch's clinical experience and academic research has been in the field of adult pulmonary disease (T.3102).

Professor Witorsch said that an important assumption underlying the epidemiological studies into the possible association between environmental tobacco exposure and respiratory function in children is that parental smoking is an adequate and reliable surrogate for direct measurement of exposure to environmental tobacco smoke of the children whose respiratory condition is being examined. He agreed that a number of the studies reported an association between parental (usually maternal) smoking and an increased frequency of respiratory symptoms and/or illness in infants and children below the age of 2 years. . He said that while individual studies suffered from various methodologic and other problems, the overall data nevertheless showed an association between maternal smoking and respiratory symptoms and/or illness in this age group of children. However, he thought there were no studies that establish any association between these findings and the development of respiratory disease or dysfunction in later life.

2021550845

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Professor Witorsch made some criticisms of the studies tendered by the applicant (especially one by Professor Landau and Dr Le Soeuf) and drew attention to the possibility of confounding factors. However, it is fairly clear from his evidence that whilst he has reservations as to the effect of passive smoking on children over the age of 12 months, he accepts that in their first year of life children of smoking mothers are more likely to have respiratory problems than children of non-smoking mothers. (T.3085). He also said that he did not see any substantial difference in the evidence on this matter between 1986 and the present time (T.3086).

He thought that socio-economic factors may account, at least in part, for the increased frequency of respiratory symptoms and illness in young children associated with maternal smoking. Parental smoking is higher in lower income groups and is also positively correlated with a number of socio-economic related variables that can adversely affect childhood respiratory health, e.g. diet, housing, living density, ventilation, personal hygiene and other health habits, cooking and heating practices. He thought that in the studies associating parental smoking with respiratory health in young children adjustments for socio-economic status were either not performed or the complexities of them were not adequately taken into consideration. In this respect he pointed to the findings in the Harlap and Davies study that while there was an increased incidence of respiratory illness, there were also increased hospitalisations due to poisoning and injury in infants of smoking parents. This suggested to Professor Witorsch that the association reported in that study, and perhaps some of the other studies, may have been indicative of general parental neglect.

2021550846

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

I do not think the socio-economic factors to which the professor referred would have been likely to have so substantially affected the results of the study showing the effect of passive smoking on very young infants as to render those results unreliable.

(f) Professor Huber

I have referred to Professor Huber's experience and qualifications elsewhere in these reasons. He does not appear to have had any special qualifications or experience in relation to respiratory disease in young children.

The professor commented upon many of the primary articles dealing with the association between environmental tobacco smoke and pulmonary functions. So far as they related to children, he said that the published results were neither uniform nor consistent and were difficult to interpret. In his proof of evidence he said little as to the effect of passive smoking on very young children, or as to the studies of such children. He made no mention of the Harlap and Davies study. With respect to the study by Fergusson et al, he thought that it did not define the precise nature of the outcomes which were being investigated. He said that in that study a child was defined as displaying symptoms of lower respiratory illness if he had received medical attention for bronchitis/pneumonia or if his mother reported "chesty colds or wheeze". He thought this definition lacked reliability and that, in any event, wheeze is usually not associated with lowers respiratory tract illness. He also thought that the reliability of the index used to define bronchitis or pneumonia was unreliable.

2021550847

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

I do not agree with these criticisms of the Fergusson et al report, which were not made by other witnesses. The authors of the Fergusson et al. report were paediatricians and might be expected to have defined with reasonable precision the nature of the outcomes they were investigating. In his analysis of the studies, the Surgeon General makes no mention of the criticisms raised by Professor Huber.

Professor Huber said (Ex. 60, p.44) there is an approximately equal number of studies which report no significant association between parental smoking and respiratory illness in children, and cited a large number of articles in support of this argument. The two studies of which he made particular mention, viz. a study conducted in Holland by Kerrebijn et al. and published in 1977 and a study by Schilling et al. carried out in the United States and published in 1977, related to respiratory symptoms in school-age children. The subjects of the Schilling study were aged seven years or more and the children studied in the Kerrebijn study were attending school.

I have read all the studies referred to by Professor Huber and I do not think they provide data which is inconsistent with the findings by Harlap and Davies and by Fergusson et al. Professor Huber did not refer to any clinical experience which he had in treating very young children.

Upon examination, some of the studies referred to by Professor Huber, but not elaborated upon in oral evidence, do not support his opinions. For instance, in a study by Bouhuys the statement is made that:

2021550848

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

"Children of smoking parents may suffer unduly from respiratory disease. For example, infants of mothers who smoke have significantly more attacks of bronchitis and pneumonia than infants of nonsmoking mothers. Also, children of smoking parents who may or may not have symptoms themselves have more bronchitis and pneumonia during their first year of life than children of nonsmoking parents. However, this was not true during four subsequent years of follow-up. But even older children may have an increased incidence of acute respiratory disease in homes where cigarettes are smoked. These studies have led to the conclusion that passive smoking (inhaling other people's smoke) is injurious to health."

The studies referred to in the above quotation are ones which were not made by Bouhuys but it is plain that he adopts them. At the time of writing the paper, Bouhuys was Professor of Medicine and Epidemiology at Yale University Lung Research Center.

The Bouhuys study was concerned with children between the ages of 7 and 18. It is true that Bouhuys concluded that exposure to low levels of smoke produced by cigarette smokers does not result in chronic respiratory symptoms among children and adults. However, it is plain that this conclusion does not relate to children in the first year or two of life.

Another study referred to by Dr Huber was that by Gardner et al. This was a relatively small study of 131 infants. The authors found that the infants of parents who smoked were not at greater risk for viral infection or respiratory illness, the only exception to this being a significant relationship between pneumonia and parental smoking, especially in mothers at home. The authors state that their observations are in contrast with those of Harlap and Davies and Leeder. It was a much smaller study than the Harlap and Davies and Fergusson studies. Most of the

2021550849

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

studies referred to by Professor Huber seem to me to have very little, if any, relevance to a consideration of the effects of passive smoking on children in the first year or two of life.

I formed the opinion that Professor Huber sees difficulties and limitations in studies which are not perceived by competent researchers and specialists in the field.

(iv) Does cigarette smoke cause respiratory disease in young children?

In my opinion the only conclusion open on the evidence is that the statement that there was little evidence and nothing which proves scientifically that cigarette smoke causes disease in non-smokers, was demonstrably false in 1986 insofar as it applied to respiratory disease in children in the first year of life. The statement remains false to this day. In my view the falsity of the statement is demonstrated whatever meaning one gives to the terms "little evidence" and "scientific proof". I share the opinion expressed by Professor Phelan that the evidence, establishing a causal relationship between passive smoking and respiratory disease in very young children is overwhelming. The evidence is of such strength that it constitutes scientific proof.

The evidence is of two kinds, epidemiological and clinical. I cannot help observing that none of the witnesses called by the respondent were specialist paediatricians or epidemiologists. On the other hand, the applicant's witnesses included specialists in both fields. I think that the respondent would have called

2021550850

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

specialists in these fields, of whom there must be many in this country and overseas, had they been able to give evidence favourable to the respondent's case.

I was greatly impressed by the applicant's witnesses and prefer to accept their opinions whenever they are in conflict with the opinions expressed by the respondent's witnesses.

As I have observed, the applicant tendered many primary articles and called much oral evidence in support of its claim that passive smoking causes respiratory disease and loss of lung function in older children and adults. I make no finding one way or the other on this part of the applicant's case, since it is unnecessary to do so for the purposes of deciding whether the advertisement is misleading or deceptive. To have dealt adequately with the evidence on this issue would have greatly expanded these already lengthy reasons.

(9) Asthma

It is part of the applicant's case that the statement in para. 3 of the advertisement is misleading or deceptive in so far as it applies to the disease of asthma. In order to evaluate this part of the case it is necessary to make brief mention of the nature and symptoms of the disease.

(i) Meaning of "asthma"

Dr Breslin, to whose evidence I shall subsequently refer in greater detail, said that the standard definition of asthma is "paroxysmal generalised airways

2021550851

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

obstruction which varies spontaneously or as a result of treatment" (T.569). He explained the disease in the following terms (T.569-70):

> *"Now, basically what asthma is it is a narrowing of the airways. The lungs are composed of two parts the breathing tubes that take air down into the spongy tissue or the lungs and the spongy tissue itself which is the lung substance. And asthma is a disease of the airways and not of the lung tissue.*
>
> *I liken it - the lung structure to say an inverted tree where you have got the trunk of the tree representing the trachea, the branches of the tree representing the remaining tubes that conduct air and the leaves of the tree being that part of the lung tissue where gas exchange takes place, oxygen is taken up by the body, carbon dioxide given off. The trunk of the tree is the trachea, the various branches are the bronchi, that gets smaller and smaller and smaller and smaller as they go out towards the leaves or alveoli and basically asthma is a disease of the conducting airways. It is not a disease of the leaves or alveoli. The basic abnormality in asthma is that out of the blue and from time to time in some patients and all the time in others the airways narrow down and then later on open up either spontaneously or as a result of treatment. Some people when a door slams leap out of their chair, some people cry easily, some people blush easily, asthmatics' airways narrow down easily. The reason they narrow down easily is because they are twitchy or hypersensitive. So one of the basic abnormalities in asthma is that the airways are twitchy. ... The airways are twitchy but having twitchy airways alone does not mean you have got asthma because there are normal people wandering around the community, probably some people in this room, who have twitchy airways but do not have asthma. In order to have asthma, the disease asthma, you need what I originally referred to in the definition and that is paroxysmal generalized airways obstruction. In addition to the twitchiness you, as it were, need the door to slam and have you leap out of the chair as it were ..."*

Having said that the airways vary from a centimetre in width at the trachea down to the width of a thread of cotton, Dr Breslin said (T.571):

> *"And these airways in asthmatics narrow down because they are twitchy and they narrow down to a variety of stimuli. So when a person has, firstly, twitchy airways and secondly, episodes of wheeze, chest tightness, shortness of breath and measurable objective changes of their lung function, then we call them asthmatic, they have the disease asthma. Having the twitchy airways in itself is not a disease because a lot of people without disease have that."*

2021550852

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Dr Breslin's description of asthma was not challenged in cross examination and I did not understand the respondent's witnesses to disagree with it.

(ii) Oral evidence

(a) Dr Breslin

Dr Antony Breslin is a consultant thoracic physician. Since 1973 he has been the Senior Specialist in Charge (Chest Diseases) at the Repatriation General Hospital, Concord. He has for many years been a lecturer at the University of Sydney. He is a former chairman of the Thoracic Society of Australia (New South Wales) Branch and a member of the Court of Clinical Examiners, Royal Australasian College of Physicians. Dr Breslin has been specialising in respiratory disease and, in particular, asthma, for about 20 years.

Dr Breslin said that unless a person has attacks of asthma he does not have the disease of asthma (T.650). It was put to him in cross examination that there is a distinction between the disease of asthma and attacks of asthma but he refused to accept this distinction. He supported his refusal by drawing a comparison between asthma and epilepsy. He said:

> *"You can have the propensity to epilepsy but if you do not have fits you do not have epilepsy. You can have the propensity to attacks but if you do not have attacks you do not have asthma."*

In his practice as a respiratory physician Dr Breslin sees a large number of patients of all ages suffering from bronchial asthma. A very large proportion of these patients indicate to him that passive smoking is harmful to their asthma and produces a deterioration in their asthmatic condition.

2021550853

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

In order to confirm whether the views of his patients could be supported objectively, Dr Breslin undertook a small study of asthmatic patients and exposed them to cigarette smoke. This study was carried out in 1984 and the results of it were published, in abbreviated form, in the Medical Journal of Australia in February 1985. The abstract of the study as published reads as follows:

> *"A study of the effect of passive smoking on patients with asthma is presented. Six patients were exposed for one hour to the air in a room in which tobacco smoke was produced mechanically over that period. The effects on symptoms, lung function and airways sensitivity to inhaled histamine were then measured and compared with the same patient's responses during a control day when they inhaled smoke-free air. All six patients developed chest tightness and symptoms similar to an attack of asthma. The findings of respiratory and sensitivity tests suggest: (i) that passive smoking may trigger asthma attacks in subjects who suffer from asthma and (ii) that the airways of such subjects show increased histamine reactivity four hours after the passive smoke exposure."*

Dr Breslin said that his clinical experience since he carried out his study in 1984 has served to confirm even more forcibly his opinion that passive smoking is a medical hazard. He said he was convinced that there is a large volume of evidence confirming that passive smoking "is a frequent and very troublesome trigger for bronchial asthma in many patients".

Dr Breslin said that about 20% of children under the age of 20 and about 10% of the total Australian population have asthma. His practice is to initially ask his patients what sort of things they have noticed trigger their asthma and then he subsequently asks them directly whether other things, which he nominates, trigger it. Thirty to thirty-five per cent of patients volunteer that cigarette smoke appears to have an effect on their asthma. When patients are specifically asked whether

2021550854

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

cigarette smoke has an effect on their asthma, the percentage of patients who respond positively rises to the order of 50 or 60% (T.582).

Dr Breslin supported his opinion by reference to articles which had appeared in learned scientific journals. One such article by Dahms et al. was published in November 1981. The authors concluded that:

> *"The results of this initial investigation indicate that patients with bronchial asthma do respond adversely when actively exposed to environmental tobacco smoke."*

There is some inconsistency among the studies referred to by Dr Breslin. One reason for the inconsistencies, as is observed in the NRC report at p. 215, is the small sample sizes in the various studies. Further, as is noted in the report, the persons surveyed were not unaware of the presence of environmental tobacco smoke and therefore the authors could not exclude the possibility that pulmonary function changes could have been emotionally related to cigarette smoke exposure, especially in those patients who reported previous histories of adverse response to exposure to environmental tobacco smoke.

In the Surgeon General's 1986 report the statement is made that biases in observation and in the selection of subjects and the subjects' own expectations may have accounted for the divergent results. However, there is nothing in the major reviews to refute Dr Breslin's evidence that cigarette smoke causes attacks of asthma in some asthmatics.

2021550855

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Dr Breslin also referred to a study carried out by Kauffmann et al. the results of which were published in the American Review of Respiratory Diseases in 1986. He said the study showed that there was a statistically significant worsening of airways obstruction in asthmatic women as a result of exposure to cigarette smoke. Also, the study demonstrated that the greater the exposure to passive smoke, the worse was the effect on the asthma of the women.

Dr Breslin also referred to a study carried out by Murray et al., the results of which were published in July 1986. The authors summarised their findings as follows:

> *"The effect of parental smoking was assessed in 94 consecutively observed children, aged 7 to 17 years, who had a history of asthmatic wheezing. The 24 children whose mothers smoked, when they were compared with children whose mothers did not smoke, had 47% more symptoms, a 13% lower mean FEV percent, a 23% lower mean FEF, and fourfold greater responsiveness to aerosolized histamine. A dose response was evident. There was a highly significant correlation between the results of the tests and the number of cigarettes the mother smoked while she was in the house. The differences between the children of smoking and nonsmoking mothers were greater in older than in younger subjects. The smoking habits of the father were not correlated with the severity of the child's asthma."*

FEV refers to forced expiratory volume. Thus FEV 1 represents the amount of air that a person can get out of his lungs in a forced manoeuvre from full inspiration in the first second. FVC means forced vital capacity, that is, the total amount of air that one can expel in one forced manoeuvre. Normally FEV 1 should be greater than 80% of the FVC. That is to say, normally if a person takes a full deep breath and then exhales rapidly and to completion he should be able to exhale more than 80% of the air in the first second. It is a characteristic of asthmatics that the ratio of their FEV 1 to their FVC during an attack of asthma is less than 80%.

2021550856

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

This is because their airways are obstructed. The use of histamine is one way of measuring the twitchiness of airways. If a normal person inhales histamine, his airways will narrow, but the airways of an asthmatic will narrow in response to a much smaller dose of histamine than is required to produce a similar reaction in a normal non-asthmatic person.

Murray et al. made the following observation on their study:

"*The evidence suggests that it is airborne cigarette smoke that causes the adverse effect. Not only is there a strong association between maternal smoking and severity of the child's asthma, but there is also evidence of a dose response. We found a significant correlation between all indicators of asthma severity and the logarithm of the number of cigarettes the mother smoked while she was in the home. There was also evidence that length of exposure had an effect. The older children, who had presumably been exposed to cigarette smoke for more years than the younger ones, were more severely affected. This finding is similar to that of Tager et al. They reported that the normal rate of increase in FEV_1 during adolescent growth is slowed in children whose mothers smoked. Further evidence, that it is passively inhaled smoke that is responsible for the changes, is the effect observed when the mother stops smoking. Vedal et al. report that children whose mothers are current smokers do but children whose mothers are exsmokers do not have significant differences in pulmonary function from those whose mothers are nonsmokers.*

In contrast to the smoking habits of the mother, those of the father had no significant correlation with the severity of the child's asthma. These findings agree with those in more recently published large epidemiologic studies. Several factors may account for this apparent paradox. One is our finding that the father, compared with the mother, smokes significantly fewer cigarettes when he is at home. Another is the possibility that the mother, more frequently than the father, is in the same room as the child when she smokes a cigarette. A third possibility is that the number of cigarettes smoked in the house are more accurately reported for the mother than for the father. The mother was usually the person who gave the information. Whatever the reason, the father's smoke did not appear to influence the child's asthma significantly. When we examined the effect of maternal and paternal smoking together, therefore, we found it to be less clear than when we examined the result of maternal smoking alone. This observation may explain the lack of effect of parental smoking on wheezing and spirometric values reported in some epidemiologic studies.

2021550857

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

....

Our findings indicate that maternal smoking aggravates asthma in children, the effect being clinically important as well as statistically significant."

Dr Breslin also supported his opinion by reference to a study by O'Connell and Logan published in 1971. The summary of the findings in this study is as follows:

"The relationship between childhood asthma and parental smoking was studied in 400 cases. The incidence of parental smoking was about the same in asthmatic children's homes as in those of controls. Tobacco smoke aggravated the asthma in 50% of all the asthmatic children and in 67% of those whose parents smoked. Exposure to tobacco smoke was considered a significant factor in 10%. Elimination was usually followed by clinical improvement."

As part of their study, O'Connell and Logan noted the effect of the cessation of parental smoking. They identified 37 children whose parents' smoking had a significantly adverse effect on their asthma. Of these 37 families, 35 were followed up six months to two years later. Among them, 20 had succeeded in stopping the children's exposure to smoke and improvement had been obtained in 18 of the children. Smoke exposure had continued in 15 of the families and improvement had occurred in only 4 of those families. The improvement in these four cases was attributed to the elimination of contact with other factors. The authors noted that in general where smoke exposure was a significant factor in asthma, its elimination was followed by improvement and with continuance of exposure improvement did not occur.

2021550858

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

O'Connell and Logan observed:

> *"From this study we assume that nearly two of every three children seen in the offices of Midwestern paediatricians come from homes in which one or both parents smoke and that, among asthmatic children from such homes, this daily air pollution aggravates the asthma at least occasionally in 67%."*

Dr Breslin acknowledged that this study had the weakness of being retrospective. The authors carried out their study by examination of clinical files and records of 400 asthmatic children who were treated for their asthma in 1969, 1970 and early 1971.

Dr Breslin referred in his evidence to a study by Shepherd. This study was not confined to persons suffering only from asthma. It included sufferers from chronic bronchitis and pulmonary emphysema. Dr Breslin described this as a "critical fault" in the study. The study considered 14 volunteer asthmatic subjects who were exposed to environmental tobacco smoke in a room. All the subjects developed some symptoms but there were only very slight changes in respiratory function tests. Four of the fourteen who gave a positive pre-test history of their asthma being worsened by exposure to passive smoking showed small changes in their FEV_1, but the others did not. Dr Breslin thought it was hard to attach any significance to the study (T.602-3).

Dr Breslin also referred to a study by Wiedemann et al. undertaken in 1983 but published in February 1986. The authors studied the acute effects of one hour of passive cigarette smoking on the lung function and airway activity of 9 young asthmatic volunteers. At the time of the study, the subjects were asymptomatic and

2021550859

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

had normal or nearly normal lung function. Passive smoking produced no change in their expiratory flow rate. The authors concluded that passive smoking presented no acute respiratory risk to young asymptomatic asthmatic patients. Dr Breslin observed of this study that it was made of subjects whom he described as "extremely mild asthmatics", none of whom was receiving any treatment. He drew a distinction between such persons and the type of persons referred to in the other studies.

Dr Breslin maintained that a person is an asthmatic if he gets attacks of asthma. He described asthma as a "recurrent condition" (T.623). His clinical experience in treating asthmatic children was not challenged, nor was his evidence as to the percentage of his patients who informed him that tobacco smoke appears to have an effect on their asthma.

(b) Professor Phelan

Professor Phelan said that passive exposure to cigarette smoke seems to have a significant effect on asthmatic symptoms, and that cessation of smoking by parents leads to an improvement in asthmatic symptoms. As to the general nature of asthma, the professor said (T.989-90):

> *"I like to think of asthma as an inherited predisposition to the development of the condition or disease called asthma. It clearly is an inherited predisposition in the airways. Then various trigger factors can lead to narrowing in those airways that results in the symptoms of asthma and to be (sic) asthma is a disease causing symptoms that interfere with the patient's normal activities - cough, wheeze and breathlessness. Between those overt symptoms there may be some degree of airways narrowing persisting but it may not be of sufficient degree to affect their day to day activities and that term may then be called subclinical asthma or - the propensity to asthma in children, we do not have adequate data to say 'Is there changes present all the time in the child who has, say, three or four*

2021550860

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

episodes of asthma a year.' To obtain that information would require to take pieces of the lining of the airways and that is ethically unacceptable in children. I think there is much evidence to suggest that three quarters of children probably have normal airways between their episodes and those episodes then are triggered by various factors."

He later said (T.990):

"... there are perhaps 20 to 30 per cent of the population [who] with appropriate trigger factors may develop allergic manifestations. It may be hay fever, it may be skin weals. Most of the time they are free of all symptoms but when they are exposed to a particular trigger factor, it may be a grass pollen, it may be an animal hair, they will develop symptoms of that condition. Now, they have allergic disease when they have those symptoms but when they are free of the symptoms I find it hard to call - say they have allergic disease as disease relates to something that is impairing bodily function."

As well as referring to some of the epidemiological studies referred to by Dr Breslin, Professor Phelan referred to a study by Horwood et al. published in 1985. This was a study carried out in New Zealand in which no evidence was found to suggest that parental smoking played a significant role in the development of asthma in children up to the age of six years. Professor Phelan said that the number of children studied was small, there being only four girls with asthma from families in which both parents smoked. Nevertheless, he thought the study, particularly in respect of boys, showed a trend, i.e. when both parents smoked there was more asthma amongst the boys than when neither parent or only one parent smoked. The same trend was not apparent amongst girls.

(c) Dr Le Souef

Dr Le Souef said that as a consultant paediatric respiratory physician he has seen many children, mostly asthmatic individuals over five or six years of age, who

2021550861

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

report that cigarette smoke exacerbates their respiratory symptoms. These children usually add that they seek cleaner air by moving away from smokers. However, more than half the children he sees are younger than this and are unable to recognise and report such associations. He said that these younger children were then more likely to remain in the vicinity of smokers, particularly infants who are held by a smoker or are too young to be mobile. It is his opinion that there are several infants under his care who have required hospitalisation due to their parents' cigarette smoke.

(d) Professor Witorsch

Professor Witorsch drew a distinction between asthma and an attack of asthma. He thought that "one is really a subdivision or a part of the other" (T.3093). He said that environmental tobacco smoke does not cause the disease of asthma but that it may produce or exacerbate symptoms in some asthmatics.

It seems to me that the difference between Professor Witorsch and Dr Breslin on the question of asthma is really one of semantics. They appear to agree that environmental tobacco smoke produces symptoms of asthma in some persons. But Professor Witorsch regards smoke as causing attacks of asthma, whereas Dr Breslin regards it as causing asthma.

I gained the impression that Professor Witorsch's experience in this field is much less than Dr Breslin's.

2021550862

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Professor Witorsch conceded that some individuals with asthma may have attacks that are precipitated by environmental tobacco smoke (T.3092). He also agreed that when some asthmatic patients are asked what causes them to have acute attacks of asthma they include environmental tobacco smoke amongst the causes (T.3099). He also agreed that the word "disease" can be taken to refer to, inter alia, acute disease and latent disease. I think it is difficult to say that an attack of asthma sustained by a person who suffers from an underlying condition of asthma does not constitute an episode of a latent disease.

(e) Professor Huber

I have referred elsewhere to Professor Huber's qualifications. Although they are extensive in the field of respiratory disease, he does not appear to have had any specialist experience in the field of asthma.

He is of the opinion that there is no reliable evidence that inhalation of environmental tobacco smoke causes asthma. He agreed that exposure to such smoke may provoke a reaction within the airways in some individuals who are already asthmatic. But he thought even that was uncertain. He thinks that when such reactions appear to occur it is unclear whether they are caused by an irritating effect of smoke on the airways or are psychological in origin. He said that even the sight of tobacco smoke may produce a reaction in some asthmatics. He thinks there is no evidence clearly indicating that a true allergic reaction occurs as a result of the inhalation of environmental tobacco smoke.

2021550863

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

Professor Huber thinks that because psychological factors are known to produce bronchospasm in asthmatics, it is quite possible that the decrease in pulmonary function noted in some asthmatics in some of the studies can be related to the psychological factors associated with the experimental design used in the studies.

Professor Huber made no comment on Dr Breslin's evidence, based on his clinical experience, as to the proportion of his patients who identify tobacco smoke as being associated with attacks of asthma.

Professor Huber's evidence included the following (T.3735):

"Do you hold any opinion as to whether it is wise for an asthmatic child to be kept for any period of time in a smoking environment, smoky (sic) meaning environmental tobacco smoke environment?---I would not recommend that they be in a smoking environment.

Why would that be?---Because some of these children will react to the irritating effects of a smoking environment and have an exacerbation of their asthma. ..."

Further, at T.3737:

"[E]xposure to environmental tobacco smoke can in some persons who are sensitive to it convert them from being someone with underlying asthma in respect of which they feel no symptoms to a person experiencing an acute attack of asthma in which they are constantly aware of symptoms?---Yes."

(iii) Conclusion on Asthma

There is overwhelming evidence, which is really not disputed by the respondent, that passive smoking causes some people to experience attacks of asthma. It is unnecessary to have regard to any of the epidemiological studies to prove that

2021550864

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

this is the case. However, the majority of the studies support the opinions expressed by the applicant's witnesses. As I have shown, the respondent's witnesses themselves virtually concede that cigarette smoke may trigger attacks of asthma.

On the other hand, the applicant has not shown that cigarette smoke of itself causes what might be described as the underlying condition of asthma.

The real question on this part of the case is whether one should characterise an attack of asthma as "disease" for the purposes of the statement made in para. 3 of the advertisement.

Dr Nolan, was asked what was his understanding of the word "disease". He said that, broadly speaking, disease could be considered to be anything that is an unhealthy process. He said:

> *"... in general I guess the term 'disease' implies a degree of disability or functional impairment, or discomfort, which is inconsistent with the notion of health."*
>
> (T.749)

This seems to me to be a reasonably workable definition of the term, and coincides broadly with the ordinary meaning of the word and also with the meaning which I think would be attached to it by the reader of the advertisement. In the context of the advertisement, the most apposite meaning of the word as given in the Shorter Oxford English Dictionary is:

2021550865

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

"A condition of the body, or of some part or organ of the body, in which its functions are disturbed or deranged."

The Macquarie Dictionary, revised edition, gives as the primary meaning of "disease":

"A morbid condition of the body, or of some organ or part; illness; sickness; ailment."

It seems to me that an attack of asthma fits easily within the dictionary definitions quoted above. Wheezing, which is one of the main symptoms of asthma, is plainly a condition of the body in which its functions are disturbed, often to a serious degree. I would think many lay persons would not distinguish between asthma and an attack of asthma. Those who did would, I think, regard the underlying condition of asthma referred to in some of the evidence as a latent disease and an attack of asthma as an acute manifestation of the disease. If such persons were told that there is little evidence and nothing which proves scientifically that cigarette smoke causes disease in non-smokers they may well be misled or deceived into believing that there is little evidence and nothing which proves scientifically that cigarette smoke causes attacks of asthma in non-smokers.

The likelihood of this happening is increased because, in its totality, the advertisement is directed at allaying the concerns of people that cigarette smoke may affect the health of non-smokers. Thus, people who are prone to asthma attacks could reasonably gain the impression from the statement made in para. 3 that they

2021550866

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

are not at risk of suffering attacks of asthma by reason of being exposed to cigarette smoke.

I accept Dr Breslin's evidence as to the nature and characteristics of asthma and of asthma attacks. I think there is much common sense in his approach that a person does not have asthma when he is not having an attack of asthma.

In my opinion the applicant's witnesses (particularly Dr Breslin) have a great deal more experience with asthma than the respondent's witnesses. Where there are differences in the opinions of the experts in this field, the opinions of the applicant's experts are to be preferred.

The evidence that cigarette smoke causes attacks of asthma is so overwhelming that I cannot accept that the draftsman of the advertisement held an opinion to the contrary. No rational basis exists for the holding of an opinion that there is little evidence and nothing which proves scientifically that cigarette smoke causes attacks of asthma. It was not suggested, nor could it have been, that any scientist could properly hold such an opinion.

I am satisfied that the applicant has established that the statement made in para. 3 of the advertisement is misleading and deceptive in so far as it applies to the disease of asthma. This is so whether the relevant date be regarded as 1 July 1986 or at any date thereafter.

2021550867

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

(10) Otitis Media

(i) Nature of the disease

The disease of chronic secretory otitis media is also known as middle ear effusion and "glue ear". It occurs when cells in the middle ear secrete abnormal amounts of a gluey substance which is then trapped in the middle ear. The resulting blockage can cause temporary deafness in children, and may require surgery to ventilate and drain the middle ear. According to Dr Nolan the result of the disease process is deafness in children which in turn has been shown to interfere with child development and learning. He said it is quite a significant disability for a child to have. It may be prolonged but it is not a permanent effect on the nerve cells of the auditory nerve. The effect of the disease is to impede transmission of sound waves into the middle ear and then to the auditory nerve.

Dr Nolan thinks that it is probable that involuntary exposure to cigarette smoke causes chronic secretory otitis media.

(ii) Primary Articles

(a) Kraemer et al. - Risk Factors for Persistent Middle-Ear effusions. Otitis Media, Catarrh, Cigarette Smoke Exposure and Atopy

The authors of this article came from the Children's Orthopedic Hospital and Medical Centre and the University of Washington School of Medicine, Seattle. It was published in the Journal of the American Medical Association in 1983.

2021550868

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

The abstract published with the study reads as follows:

"To ascertain risk factors for persistent middle-ear effusions (PMEE), we interviewed the parents of two groups of children. The first consisted of 76 children with PMEE who were admitted to the hospital for tympanostomy-tube insertion. The second, a control group, consisted of 76 children admitted for other types of surgery, who were matched for age, sex, season, and surgical ward. Nearly all (97%) of the children admitted for insertion of tympanostomy tubes had one or more episodes of suppurative otitis media. Only 59% of the control children had previous ear infections. Frequent ear infections sharply increased the risk for persistent effusions. Catarrh, household cigarette smoke exposure, and atopy also occurred more frequently in children with PMEE. The risk for middle-ear effusions was greatest when these three factors were all present. The avoidance of daily exposure to domestic tobacco smoke and, if atopic, of specific allergens should be included in the medical treatment of children with PMEE."

Table I on p.1023 of the study sets out the relative risk of persistent middle-ear effusions according to the different variables about which information was obtained during interview. These variables included racial background, family size, frequency of catarrh, atopic disease, frequency of suppurative otitis media and household exposure to cigarette smoke.

.../202

2021550869

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

An extract from the table dealing with household cigarette exposure is set out below:

Characteristic	No. (%) of PMEE Cases (N=76)	No. (%) of Surgical Control Subjects (N=76)	Relative Risk	95% Confidence Interval
Household cigarette smokers				
0	38 (50.0)	45 (59.2)	1.0	-
1	19 (25.0)	23 (30.3)	1.0	0.5-2.1
≥ 2	19 (25.0)	8 (10.5)	2.6	1.1-7.0
Household cigarette use No. packs per day				
None	38 (50.0)	45 (59.2)	1.0	-
01. - 0.9	11 (14.5)	7 (9.2)	1.9	0.7-5.3
1.0 - 1.9	13 (17.1)	14 (18.4)	1.1	0.5-2.6
2.0 - 2.9	7 (9.2)	8 (10.5)	1.0	0.3-3.1
≥ 3.0	7 (9.2)	2 (2.6)	4.1	0.9-19.2

This extract shows that a statistically significant relative risk of 2.6 was found for cases where there were 2 or more cigarette smokers in the household, but no increase in risk was found where there was one household smoker. It also shows that when exposure was measured by packs per day a linear dose response relationship was not apparent and no subgroup result was statistically significant. However when household cigarette use equalled or exceeded 3 packs per day, the

2021550870

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

relative risk of persistent middle-ear effusion was reported as 4.1 (95% C.I. 0.9 - 19.2).

A later table in the study shows the combined effects of nasal congestion, cigarette smoke exposure, and atopy. The authors reported that:

> *"[N]asal congestion alone elevated the risk nearly fourfold. When cigarette smoke exposure or atopy was added to nasal congestion, the risk increased. Children with all three factors were more than six times as likely to manifest PMEE."*

(b) Black - The Aetiology of Glue Ear - A Case-Control Study

The author of this study was from the Department of Community Medicine and General Practice at Oxford University. The article was published in the International Journal of Pediatric Otorhinolaryngology in 1985.

The abstract published with the study reads as follows:

> *"A case-control study was carried out to investigate many of the proposed causes of glue ear in childhood. One hundred and fifty cases with two matched controls were found to be remarkably similar in nearly all medical and social aspects of their past and present lives, thus providing no support for many of the currently held views on the aetiology of glue ear. Of the 5 factors which were found to increase the risk of a child undergoing surgery for glue ear, only one of these is thought to be related to the development of the condition, rather than to the chances of its detection. This factor was parental smoking (RR 1.64) ...."*

The author stated:

> *"A significant association was found (RR 1.64; $P < 0.05$) between glue ear and the smoking habits of all household members throughout the subject's*

2021550871

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000

life. This analysis assumes a constant level of exposure to smoke throughout the subject's life. Further study would be required to determine whether or not the risk of smoke is associated with any particular stage of childhood."

(p.131)

The statistically significant result of 1.64 emerged after original insignificant results were subjected to further (matched pair) analysis. It was suggested to Professor Landau in cross-examination that this was a weak association and that the author was attempting to use two reported weak associations to argue for a strong association. Professor Landau said that the conclusion of a strong association was based on the consistent findings. However, he agreed that the Black study (and also Kraemer's) showed no more than that cigarette smoke was a risk factor for glue ear.

The respondent led no expert evidence directly on the issue of otitis media and environmental tobacco smoke.

(iii) The major reviews

The authors of the N.R.C. report state (at p.274):

"Household exposure to ETS is linked with increased rates of chronic ear infections and middle-ear effusions in young children. For children with nasal allergies and recurrent otitis media, ETS exposure may synergistically increase their risk of persistent middle-ear effusions."

2021550872

Source: https://www.industrydocuments.ucsf.edu/docs/sxvl0000